

WEST Search History

DATE: Thursday, July 27, 2006

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
		<i>DB=PGPB,USPT; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	Forbes adj Briony	1

END OF SEARCH HISTORY

WEST Search History

DATE: Thursday, July 27, 2006

Hide?	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB, USPT; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L3	L2 and (extracellular adj matrix)	234
<input type="checkbox"/>	L2	insulin adj like adj growth adj factor adj binding adj protein? and (alteration? or variant? or mutein?)	537

END OF SEARCH HISTORY

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=> file medline

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SINCE FILE ENTRY	TOTAL SESSION
0 21	0 21

FILE LAST UPDATED: 26 Jul 2006 (20060726/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).

See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s tu insulin(w)like(w)growth(w)factor(w)binding(w)protein(w)2 or IGFBP-2
    1233632 TU
        217 TUS
    1233807 TU
        (TU OR TUS)
    210372 INSULIN
        1485 INSULINS
    210398 INSULIN
        (INSULIN OR INSULINS)
        0 TU INSULIN
            (TU(W) INSULIN)
    379034 LIKE
        239 LIKES
    379236 LIKE
        (LIKE OR LIKES)
    845215 GROWTH
        1631 GROWTHS
    846428 GROWTH
        (GROWTH OR GROWTHS)
    757830 FACTOR
    1977653 FACTORS
    2452560 FACTOR
        (FACTOR OR FACTORS)
    772844 BINDING
        1419 BINDINGS
    773165 BINDING
        (BINDING OR BINDINGS)
    1552478 PROTEIN
    1303418 PROTEINS
    1970238 PROTEIN
        (PROTEIN OR PROTEINS)
    3320766 2
        0 TU INSULIN(W)LIKE(W)GROWTH(W)FACTOR(W)BINDING(W)PROTEIN(W)2
        5305 IGFBP
        1893 IGFBPS
        5515 IGFBP
            (IGFBP OR IGFBPS)
    3320766 2
        1370 IGFBP-2
            (IGFBP(W)2)
L1      1370 TU INSULIN(W)LIKE(W)GROWTH(W)FACTOR(W)BINDING(W)PROTEIN(W)2 OR
        IGFBP-2
```

=> s 11 and cancer
548023 CANCER
78555 CANCERS
572127 CANCER
(CANCER OR CANCERS)

L2 139 L1 AND CANCER

=> s 12 and colon
101315 COLON
1129 COLONS
612 COLA
47 COLAS
102123 COLON
(COLON OR COLONS OR COLA OR COLAS)

L3 14 L2 AND COLON

=> dis ibib abs 13 1-14

L3 ANSWER 1 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003577127 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14656210
TITLE: Interleukin-1beta (IL-1beta) and IL-6 modulate insulin-like growth factor-binding protein (IGFBP) secretion in colon cancer epithelial (Caco-2) cells.
AUTHOR: Street M E; Miraki-Moud F; Sanderson I R; Savage M O; Giovannelli G; Bernasconi S; Camacho-Hubner C
CORPORATE SOURCE: Department of Endocrinology, St Bartholomew's Hospital, London, UK.. mariaelisabeth.street@unipr.it
SOURCE: The Journal of endocrinology, (2003 Dec) Vol. 179, No. 3, pp. 405-15.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 25 Feb 2004
Entered Medline: 24 Feb 2004

AB Chronic inflammation is characterised by modifications in cytokine concentrations, whereas growth is mainly dependent on the GH-IGF axis. IGF-I bioavailability is modulated by a family of IGF-binding proteins (IGFBPs). The aim of the present study was to evaluate the interactions among interleukin-1beta (IL-1beta), IL-6 and IGFBP secretion by intestinal cells to assess whether cytokines modulate IGFBP secretion, and in turn IGF-I and IGF-II bioavailability. The human colon carcinoma derived cell line Caco-2 was used as an in vitro model for its capacity to differentiate spontaneously. Experiments were carried out on day 4 (undifferentiated state) and day 14 (differentiated state) after plating. Carcinoembryonic antigen (CEA) was used as a marker of differentiation and increased in the conditioned media (CM) from days 4 to 14 ($0.2+/-0.01$ ng/ml per 10(5) cells vs $3.3+/-0.2$ ng/ml per 10(5) cells, $P<0.05$). IGFBP-2 and IGFBP-4 secretion decreased concomitantly. Cells were stimulated with IL-1beta and IL-6 at 1, 10 and 50 ng/ml, and with IL-1beta and IL-6 in combination at the same dose of 1 and 10 ng/ml. IGF-I at 50 ng/ml was used as a control. Caco-2 cells expressed and secreted mainly IGFBP-2 and IGFBP-4 into the CM. On day 4, IL-1beta (1 ng/ml) and IL-6 (10 and 50 ng/ml) reduced IGFBP-2 by $29+/-8\%$, and by $32+/-9$ and $38+/-8\%$ respectively ($P<0.05$). IGFBP-4 was also reduced by IL-1beta at 1 and 50 ng/ml ($-14+/-4\%$ and $-46+/-11\%$ vs serum free medium (SFM) respectively, $P<0.05$), and IL-6 at 50 ng/ml ($-46+/-15\%$, $P<0.05$). Both IGFBP-2 and IGFBP-4 were reduced by IL-1beta and IL-6 in combination at 1 and 10 ng/ml ($P<0.05$). On day 14, IGFBP-2 band intensity was

reduced at 10 ng/ml of IL-1beta (-22%/-15% vs SFM, P<0.05) and at 50 ng/ml of both cytokines (-33%/-8% and -13%/-13% vs baseline respectively, P<0.05). IGFBP-4 band intensity decreased with 10 and 50 ng/ml of IL-1beta (-35%/-11% and -46%/-15% vs SFM respectively) and IL-6 (-36%/-10% and -46%/-15% vs SFM respectively). IL-1beta and IL-6 in combination at 1 and 10 ng/ml reduced both IGFBP-2 and IGFBP-4. In conclusion, IGFBP-2 and IGFBP-4 secretion in CM decreased with Caco-2 cell differentiation. IGFBP-2 and IGFBP-4 were significantly decreased by IL-1beta and IL-6 treatment in both the undifferentiated and differentiated state. Furthermore, these cytokines increased cell proliferation whereas total protein content was significantly reduced only at the higher concentrations of IL-6 and IL-1beta. These findings suggest that interleukins modulate the IGF-IGFBP system in Caco-2 cells in vitro.

L3 ANSWER 2 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003509615 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14585185
TITLE: trans-10, cis-12 conjugated linoleic acid reduces insulin-like growth factor-II secretion in HT-29 human colon cancer cells.
AUTHOR: Cho Han Jin; Lee Hyun Sook; Chung Cha-Kwon; Kang Young-Hee; Ha Yeong Lae; Park Hyun-Suh; Park Jung Han Yoon
CORPORATE SOURCE: Division of Life Sciences and Silver Biotechnology Research Center, Hallym University, Chunchon, Korea.
SOURCE: Journal of medicinal food, (2003 Fall) Vol. 6, No. 3, pp. 193-9.
Journal code: 9812512. ISSN: 1096-620X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 31 Oct 2003
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004

AB We previously demonstrated that a mixture of conjugated linoleic acid (CLA) isomers decreases colon cancer incidence in rats treated with 1,2-dimethylhydrazine. Our in vitro studies have also shown that CLA inhibits the growth of HT-29 cells, a human colon cancer cell line. When we compared the individual potencies of the two main isomers found in the mixture of CLA isomers (e.g., cis-9, trans-11 [c9t11] and trans-10, cis-12 [t10c12]), t10c12 CLA decreased viable cell numbers in a dose-dependent manner. By contrast, c9t11 CLA had no effect. Therefore, the present study examined whether the decreased cell growth is related to changes in secretion of insulin-like growth factor (IGF)-II and/or IGF-binding proteins (IGFBPs) that have been shown to regulate HT-29 cell proliferation. Cells were incubated in serum-free medium with various concentrations of the individual CLA isomers, and immunoblot analysis of 24-hour, serum-free, conditioned media using a monoclonal anti-IGF-II antibody was performed. HT-29 cells secreted both mature 7,500 apparent molecular weight (M(r)) and higher-M(r) forms of IGF-II. t10c12 CLA decreased the levels of the higher-M(r) and the mature form of IGF-II in a dose-dependent manner, whereas c9t11 CLA had no effect. Ligand blot analysis of conditioned medium using (125)I-IGF-II revealed that the production of IGFBP-2 and IGFBP-4 was also decreased by t10c12 CLA, whereas c9t11 CLA had no effect. Exogenous IGF-II abrogated the growth inhibition induced by t10c12 CLA. These results indicate that inhibition of HT-29 cell growth by t10c12 CLA may be mediated by decreasing IGF-II secretion in these cells.

L3 ANSWER 3 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003388494 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12925961
TITLE: Plasma insulin, IGF-binding proteins-1 and -2 and risk of colorectal cancer: a prospective study in northern Sweden.
AUTHOR: Palmqvist Richard; Stattin Par; Rinaldi Sabina; Biessy Carine; Stenling Roger; Riboli Elio; Hallmans Goran; Kaaks Rudolf
CORPORATE SOURCE: Department of Medical Biosciences, Umea University Hospital, Umea, Sweden.
SOURCE: International journal of cancer. Journal international du cancer, (2003 Oct 20) Vol. 107, No. 1, pp. 89-93.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20 Aug 2003
Last Updated on STN: 10 Oct 2003
Entered Medline: 9 Oct 2003

AB Chronically elevated plasma insulin levels have been postulated to increase colon cancer risk, either directly through colonic insulin receptors or indirectly through downregulation of IGFBP-1 and/or IGFBP-2, thus increasing IGF activity. Our aim was to examine the relationships of plasma insulin and IGFBPs-1 and -2 with risks of colon and rectal cancers. We conducted a case-control study nested within the prospective Northern Sweden Health and Disease Cohort. Insulin and IGFBPs were measured in prediagnostic plasma samples from 168 men and women who developed cancers of the colon ($n = 110$) or rectum ($n = 58$) and from 336 matched controls. Conditional logistic regression analyses showed no significant relationship of plasma insulin with risk of colon or rectal cancer. In subjects whose blood samples had been collected after more than 4 hr of fasting, insulin showed a moderate but still nonsignificant association with colorectal cancer risk [ORs over quartiles: 1.00, 0.70 (95% CI 0.35-1.39), 1.06 (95% CI 0.55-2.07), 1.63 (95% CI 0.82-3.24); $p(\text{trend}) = 0.10$]. Plasma IGFBP-1 and IGFBP-2 showed no association with risk of colon and/or rectal cancer, either in the full study population or among the fasting subjects. Our results only moderately support a possible relationship of chronic hyperinsulinemia with colon cancer risk.
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L3 ANSWER 4 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2002400816 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12121883
TITLE: Trans-10,cis-12-conjugated linoleic acid inhibits Caco-2 colon cancer cell growth.
AUTHOR: Kim Eun J; Holthuizen P Elly; Park Hyun S; Ha Yeong L; Jung Kyeong C; Park Jung H Y
CORPORATE SOURCE: Division of Life Sciences, Hallym University, Chunchon 200-702, Korea.
SOURCE: American journal of physiology. Gastrointestinal and liver physiology, (2002 Aug) Vol. 283, No. 2, pp. G357-67.
Journal code: 100901227. ISSN: 0193-1857.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 2 Aug 2002
Last Updated on STN: 16 Aug 2002
Entered Medline: 15 Aug 2002
AB A commercially available mixture of conjugated linoleic acid (CLA) isomers

decreases colon cancer cell growth. We compared the individual potencies of the two main isomers in this mixture [cis-9,trans-11 (c9t11) and trans-10,cis-12 (t10c12)] and assessed whether decreased cell growth is related to changes in secretion of insulin-like growth factor II (IGF-II) and/or IGF-binding proteins (IGFBPs), which regulate Caco-2 cell proliferation. Cells were incubated in serum-free medium with different concentrations of the individual CLA isomers. t10c12 CLA dose dependently decreased viable cell number (55 +/- 3% reduction 96 h after adding 5 microM t10c12 CLA). t10c12 CLA induced apoptosis and decreased DNA synthesis, whereas c9t11 CLA had no effect. Immunoblot analysis of 24-h serum-free conditioned medium using a monoclonal anti-IGF-II antibody revealed that Caco-2 cells secreted both a mature 7,500 molecular weight (M(r)) IGF-II and higher M(r) forms of IGF-II. The levels of the higher M(r) and the mature form of IGF-II were decreased 50 +/- 3% and 22 +/- 2%, respectively, by 5 microM t10c12 CLA. c9t11 CLA had no effect. Ligand blot analysis of conditioned medium using ¹²⁵I-labeled IGF-II revealed that t10c12 CLA slightly decreased IGFBP-2 production; c9t11 CLA had no effect. Exogenous IGF-II reversed t10c12 CLA-induced growth inhibition and apoptosis. These results indicate that CLA-inhibited Caco-2 cell growth is caused by t10c12 CLA and may be mediated by decreasing IGF-II secretion in Caco-2 cells.

L3 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2002081238 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11807815
TITLE: Inhibition of Caco-2 cell proliferation by all-trans retinoic acid: role of insulin-like growth factor binding protein-6.
AUTHOR: Kim Eun J; Kang Young-Hee; Schaffer Beverly S; Bach Leon A; MacDonald Richard G; Park Jung H Y
CORPORATE SOURCE: Division of Life Sciences, Institute of Environment & Life Science, Hallym University, Chunchon, 200-702, Korea.
SOURCE: Journal of cellular physiology, (2002 Jan). Vol. 190, No. 1, pp. 92-100.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 28 Jan 2002
Last Updated on STN: 1 Feb 2002
Entered Medline: 31 Jan 2002

AB The present study examined the effects of all-trans retinoic acid (tRA) on proliferation and expression of the IGF system in Caco-2 human colon adenocarcinoma cells. tRA inhibited Caco-2 cell proliferation in a dose-dependent manner, with a 40 +/- 2% decrease in cell number observed 48 h after the addition of 1 microM tRA. Ligand blot analysis of IGFBPs in conditioned media revealed that Caco-2 cells produced three IGFBPs of M(r): 34,000 (IGFBP-2), 24,000 (IGFBP-4), and 32,000 (IGFBP-6). The concentrations of IGFBP-2 and IGFBP-4 decreased by 48 +/- 6 and 70 +/- 13%, respectively, whereas that of IGFBP-6 increased by 698 +/- 20% with 1 microM tRA. tRA decreased mRNA levels of IGFBP-2 and IGFBP-4 by 20 +/- 3 and 50 +/- 8%, respectively, whereas tRA increased IGFBP-6 mRNA by 660 +/- 20%. tRA did not alter levels of IGF-II mRNA or peptide. To examine if endogenous IGFBP-6 inhibits cell proliferation, Caco-2 cells were transfected with an IGFBP-6 cDNA expression construct or pcDNA3 vector only and stable clones were selected. Clones overexpressing IGFBP-6 grew more slowly than vector controls and achieved final densities 30-55% lower than those of vector controls. Accumulation of IGFBP-6 mRNA and concentrations of IGFBP-6 peptide in conditioned media were increased by 200-250 and 220-250%, respectively, in the IGFBP-6 clones compared with controls. Increased expression of IGFBP-6, which has a high binding

affinity for IGF-II, following tRA treatment suggests that the decreased proliferation caused by tRA may result, at least in part, from IGFBP-6-mediated disruption of the IGF-II autocrine loop in these colon cancer cells.

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L3 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2001558242 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11604234
TITLE: Synthetic low-calcaemic vitamin D(3) analogues inhibit secretion of insulin-like growth factor II and stimulate production of insulin-like growth factor-binding protein-6 in conjunction with growth suppression of HT-29 colon cancer cells.
AUTHOR: Oh Y S; Kim E J; Schaffer B S; Kang Y H; Binderup L; MacDonald R G; Park J H
CORPORATE SOURCE: Division of Life Sciences and Institute of Environment and Life Science, Hallym University, 1 Okchon Dong, Chunchon, 200-702, South Korea.
SOURCE: Molecular and cellular endocrinology, (2001 Oct 25) Vol. 183, No. 1-2, pp. 141-9.
Journal code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 18 Oct 2001
Last Updated on STN: 21 Feb 2002
Entered Medline: 20 Feb 2002

AB The aims of the present study were to compare the ability of various synthetic analogues of 1 alpha,25-dihydroxyvitamin D(3) [1 alpha,25-(OH)(2)D(3)] to inhibit proliferation of HT-29 cells, a human colon adenocarcinoma cell line. HT-29 cells were incubated for 144 h with various concentrations (0-100 nM) of 1 alpha,25-(OH)(2)D(3), or the analogues EB1089, CB1093 or 1 beta,25-(OH)(2)D(3). All these analogues except 1 beta,25-(OH)(2)D(3) inhibited cell proliferation, but relative potencies and efficacies of EB1089 and CB1093 were much greater than that of the native vitamin. Cells grew in serum-free medium, reaching a plateau density at day 10 of culture, and addition of 10 nM 1 alpha,25-(OH)(2)D(3) or 1 beta,25-(OH)(2)D(3) did not alter the long-term growth characteristics of HT-29 cells. However, cells treated with 10 nM EB1089 or CB1093 grew at a rate slower than control and reached final densities that were 53+/-1 and 36+/-2% lower than control, respectively. Immunoblot analysis of serum-free conditioned medium using a monoclonal anti-insulin-like growth factor-II antibody showed that both 10 nM EB1089 and CB1093 markedly inhibited secretion of both mature 7500 M(r) and higher M(r) forms of IGF-II. Ligand blot and immunoblot analyses of conditioned media revealed the presence of IGFBPs of M(r) 24,000 (IGFBP-4), 30,000 (glycosylated IGFBP-4), 35,000 (IGFBP-2) and 32,000-34,000 (IGFBP-6). The level of IGFBP-2 was decreased by 42+/-8 and 49+/-7% by 10 nM EB 1089 and CB1093, respectively, compared to controls. IGFBP-6 was increased approximately twofold by EB1089 and CB1093, and exogenously added IGFBP-6 inhibited HT-29 cell proliferation. These results suggest that inhibition of HT-29 cell proliferation by EB1089 and CB1093 may be attributed, at least in part, to the decreased secretion of IGF-II. The increase in IGFBP-6 concentration coupled with its high affinity for IGF-II may also contribute to decreased cellular proliferation by an indirect mechanism involving sequestration of endogenously produced IGF-II.

L3 ANSWER 7 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2001050299 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11018095

TITLE: Serum C-peptide, insulin-like growth factor (IGF)-I, IGF-binding proteins, and colorectal cancer risk in women.

AUTHOR: Kaaks R; Toniolo P; Akhmedkhanov A; Lukanova A; Biessy C; Dechaud H; Rinaldi S; Zeleniuch-Jacquotte A; Shore R E; Riboli E

CORPORATE SOURCE: International Agency for Research on Cancer, Lyon, France.. kaaks@iarc.fr

SOURCE: Journal of the National Cancer Institute, (2000 Oct 4) Vol. 92, No. 19, pp. 1592-600.
Journal code: 7503089. ISSN: 0027-8874.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 14 Dec 2000

AB BACKGROUND: Leading a Western lifestyle, being overweight, and being sedentary are associated with an increased risk of colorectal cancer. Recent theories propose that the effects of these risk factors may be mediated by increases in circulating insulin levels and in the bioactivity of insulin-like growth factor (IGF)-I. To test this hypothesis, we conducted a case-control study nested within a cohort of 14 275 women in New York. METHODS: We used blood samples that had been obtained from these women from March 1985 through June 1991 and stored in a biorepository. C-peptide (a marker for insulin secretion), IGF-I, and IGF-binding proteins (IGFBPs)-1, -2, and -3 were assayed in the serum of 102 women who subsequently developed colorectal cancer and 200 matched control subjects. Logistic regression was used to relate cancer risk to these peptide levels, by adjustment for other risk factors. All statistical tests used are two-sided. RESULTS: Colorectal cancer risk increased with increasing levels of C-peptide ($P:(trend) = .001$), up to an odds ratio (OR) of 2. 92 (95% confidence interval [CI] = 1.26-6.75) for the highest versus the lowest quintiles, after adjustment for smoking. For colon cancer alone (75 case subjects and 146 control subjects), ORs increased up to 3.96 (95% CI = 1.49-10.50; $P:(trend) < .001$) for the highest versus the lowest quintiles. A statistically significant decrease in colorectal cancer risk was observed for increasing levels of IGFBP-1 ($P:(trend) = .02$; OR in the upper quintile = 0.48 [95% CI = 0.23-1. 00]), as well as for the highest quintile of IGFBP-2 levels ($P:(trend) = .06$; OR = 0.38 [95% CI = 0.15-0.94]). Colorectal cancer risk showed a modest but statistically nonsignificant positive association with levels of IGF-I and was statistically significantly increased for the highest quintile of IGFBP-3 (OR = 2.46 [95% CI = 1. 09-5.57]). CONCLUSIONS: Chronically high levels of circulating insulin and IGFs associated with a Western lifestyle may increase colorectal cancer risk, possibly by decreasing IGFBP-1 and increasing the bioactivity of IGF-I.

L3 ANSWER 8 OF 14 MEDLINE on STN

ACCESSION NUMBER: 2000456527 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10985759

TITLE: Role of insulin-like growth factor-I (IGF-I) receptor, IGF-I, and IGF binding protein-2 in human colorectal cancers.

AUTHOR: Mishra L; Bass B; Ooi B S; Sidawy A; Korman L

CORPORATE SOURCE: Department of Medicine, Department of Veterans' Affairs Medical Center and Georgetown University Medical Center, Washington DC 20422, USA.

SOURCE: Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF

Research Society, (1998 Dec) Vol. 8, No. 6, pp. 473-9.
Journal code: 9814320. ISSN: 1096-6374.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 5 Oct 2000
Last Updated on STN: 5 Oct 2000
Entered Medline: 25 Sep 2000

AB The identification of novel autocrine/paracrine signaling pathways and possible markers represents an important component in the understanding of tumor growth control. In this study, we assessed the potential role of insulin-like growth factor-I (IGF-I), the IGF-I receptor (IGF-IR) and IGF binding protein-2 (IGFBP-2) in human colorectal cancer. Initial studies demonstrating increased IGF-I binding and IGF-IR density in human colon cancer tissue revealed that a component of iodinated (3-[125-I]iodotyrosyl) IGF-I (125I-ICGF-I) binding was not attributable to IGF-IR. Binding studies and Western blot analysis suggested that this second component of 125I-IGF-I binding could be due to IGFBP-2. Further analysis by a specific solution hybridization/RNase protection assay for IGF-IR mRNA levels, IGFBP-2 mRNA levels and in situ hybridization for IGFBP-2 localization, was carried out in nine patients with colon cancer. IGF-IR mRNA levels by RNase protection assays were unchanged, whereas IGFBP-2 mRNA levels were increased 4-8-fold in patients with colon cancer compared to controls. Three patients with Dukes stage C disease had the highest levels of IGFBP-2 mRNA. In situ hybridization studies localized IGFBP-2 mRNA to malignant cells and not to the surrounding stromal cells, suggesting an autocrine role for IGFBP-2. The discrepancy between increased IGF-I binding, IGF-IR density, IGFBP-2 mRNA and the minimal modulation of the IGF-IR mRNA implies post-transcriptional regulation of IGF-IRs. Our results suggest that IGFBP-2 may be implicated in colon cancer metastases and prognosis. Its usefulness as a potential tumor marker should be further investigated.

L3 ANSWER 9 OF 14 MEDLINE on STN
ACCESSION NUMBER: 1998048232 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9386991
TITLE: Insulin-like growth factor binding proteins as mediators of IGF-I effects on colon cancer cell proliferation.
AUTHOR: Michell N P; Dent S; Langman M J; Eggo M C
CORPORATE SOURCE: Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, UK.
SOURCE: Growth factors (Chur, Switzerland), (1997) Vol. 14, No. 4, pp. 269-77.
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 17 Dec 1997

AB Human colon cancer cell lines COLO205, HT29 and SW620 are known to secrete insulin-like growth factor II (IGF-II) and its modulatory binding proteins (IGFBPs). We have characterised the sensitivity of these cell lines to exogenous IGF-I and have examined the effects of their autocrine IGFBPs on these responses. Cells cultured in

serum-free medium were treated with 1-100 ng/ml IGF-I, or des(1,3)IGF-I, a truncated IGF-I with low affinity for IGFBPs. DNA synthesis was determined by 24 h incorporation of 3H-thymidine. Experiments were repeated in the presence of 24 h cell-conditioned media containing endogenous IGFBPs. In all 3 cell lines, cell-conditioned media reduced sensitivity to IGF-I but not to des(1,3)IGF-I suggesting that IGFBPs in the cell-conditioned media of colon cells inhibit IGF-I action. IGFBPs in the cell layer and 24 h cell-conditioned media were identified by Western ligand and antibody analyses. IGFBP-4 was secreted by all cell lines and IGFBP-2 from the COLO205 and SW620 cells lines but not the HT29 cells. No IGFBP-3 was secreted by any of the cell lines but IGFBP-3 was found in the cell layer in all of the cell lines. When endogenous secreted IGFBPs were removed, cell lines were consistently more sensitive to IGF-I than des(1,3)IGF-I suggesting that IGFBP-3 associated with the cell layer enhances responses to IGF-I. This is in contrast to the effects of the secreted IGFBPs. Differential modulating actions of IGFBPs may be important in regulating colon cell turnover.

L3 ANSWER 10 OF 14 MEDLINE on STN
ACCESSION NUMBER: 97456288 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9311602
TITLE: Surface-bound plasmin induces selective proteolysis of insulin-like-growth-factor (IGF)-binding protein-4 (IGFBP-4) and promotes autocrine IGF-II bio-availability in human colon-carcinoma cells.
AUTHOR: Remacle-Bonnet M M; Garrouste F L; Pommier G J
CORPORATE SOURCE: Unite Interactions entre Systemes Proteiques et Differentiation dans la Cellule Tumorale, Faculte de Medecine, URA CNRS 1924, Marseille, France.
SOURCE: International journal of cancer. Journal international du cancer, (1997 Sep 4) Vol. 72, No. 5, pp. 835-43.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 31 Oct 1997
AB Limited proteolysis of insulin-like-growth-factor (IGF)-binding proteins (IGFBPs) represents a key process to modulate IGF bio-availability at the cellular level. In human colon carcinomas, urokinase-type plasminogen activator (u-PA) produced by stroma cells can bind to cancer-cell-associated u-PA receptor (u-PAR), and then catalyze the conversion of plasminogen (Pg) into plasmin (Pm). We therefore investigated the interplay between the IGF and Pm systems in the HT29-D4 human colon-carcinoma-cell model. HT29-D4 cells secreted IGF-II totally complexed to IGFBP-2, IGFBP-4 and IGFBP-6. Approximately 15% of IGFBP-4 was associated with the extracellular matrix. HT29-D4 cells produced neither u-PA- nor IGFBP-specific proteases. However, activation of Pm at the HT29-D4 cell surface obtained by the sequential addition of exogenous u-PA and Pg to mimic the stromal complementation induced selective proteolysis targeted to IGFBP-4 only (>95%). IGFBP-2 and IGFBP-6, though sensitive to proteolysis by soluble Pm, were not altered by cell-bound Pm. IGFBP-4 proteolysis yielded 18- and 14-kDa immunoreactive fragments which were not detectable by Western ligand blotting, indicating that they bound IGF-II with poor affinity. Release of IGF-II from IGF-II-IGFBP complexes after IGFBP-4 proteolysis by cell-bound Pm was indicated by the observation that approximately 20% of the 125I-IGF-II initially associated with endogenous IGFBP in reconstituted complexes was transferred to HT29-D4 cell-surface IGF-I receptors. These results suggest that IGFBP-4 proteolysis by

cell-bound Pm can promote autocrine/paracrine IGF-II bio-availability in colon-cancer cells. This may have important consequences on the behavior of cancer cells at the interface between stroma and malignant cells in carcinomas of the colon *in vivo*.

L3 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 97361773 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9218734
TITLE: Insulin-like growth factors and their binding proteins in human colonocytes: preferential degradation of insulin-like growth factor binding protein 2 in colonic cancers

AUTHOR: Michell N P; Langman M J; Eggo M C
CORPORATE SOURCE: Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, UK.
SOURCE: British journal of cancer, (1997) Vol. 76, No. 1, pp. 60-6.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 12 Aug 1997
Last Updated on STN: 12 Aug 1997
Entered Medline: 29 Jul 1997

AB We have compared the expression of insulin-like growth factors (IGFs) and IGF binding proteins (IGFBPs) in ten paired samples of normal and tumour colonic tissue with regard to both mRNA and protein. We have compared sensitivity of these tissues to IGF-I using primary cultures of epithelial cells of colonic mucosa, and we have examined the production of IGFs and IGFBPs by these cells. In the tissues, IGFBP-2 mRNA was expressed in all normal and cancer samples but other IGFBPs showed variable expression. mRNAs for IGF-I were expressed in all normal and cancer tissues but IGF-II mRNA was only detected in cancer tissue (3 out of 10). Immunostaining of sections of normal and cancer tissue was negative for IGF-I and IGF-II; IGFBP-2 was positive in 2 out of 10 cancer tissues and 7 out of 10 normal tissues; IGFBP-3 was positive in 7 out of 10 cancer tissues and 7 out of 10 normal tissues; and IGFBP-4 was positive in 5 out of 10 cancer tissues and 6 out of 10 normal tissues. In the cells in culture, cancer cells showed increased incorporation of [³⁵S]methionine into protein and [³H]thymidine into DNA ($P < 0.02$) when treated with IGF-I. Western blotting of serum-free conditioned media from cells in culture showed that 8 out of 10 normal and 3 out of 10 cancer cultures produced a 32-kDa immunoreactive IGFBP-2. No IGFBP-3 was secreted by any culture but 24-kDa IGFBP-4 was found in 3 out of 10 normal and 5 out of 10 cancer tissues. Because of the discrepancy between mRNA and protein expression for IGFBP-2, degradation of native IGFBPs was assessed using tissue extracts. Colon cancer extracts were able to degrade exogenous IGFBP-2, IGFBP-3 and IGFBP-4, whereas normal tissue extracts were without effect on IGFBP-2. We conclude that IGFBPs are synthesized and secreted by cells of the colonic mucosa but that proteolysis of secreted IGFBP-2 occurs in colon cancer tissue. This selective degradation may confer a growth advantage.

L3 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 96198774 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8612513
TITLE: Proliferation and differentiation of a human colon cancer cell line (CaCo2) is associated with

AUTHOR: significant changes in the expression and secretion of insulin-like growth factor (IGF) IGF-II and IGF binding protein-4: role of IGF-II.
CORPORATE SOURCE: Singh P; Dai B; Yallampalli U; Lu X; Schroy P C
Department of Anatomy and Neurosciences, University of Texas Medical Branch, Galveston 77555-1043, USA..
psingh@mbian.utmb.edu

CONTRACT NUMBER: CA-38651 (NCI)
CA-60087 (NCI)

SOURCE: Endocrinology, (1996 May) Vol. 137, No. 5, pp. 1764-74.
Journal code: 0375040. ISSN: 0013-7227.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 13 Jun 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 5 Jun 1996

AB The extent to which the insulin-like growth factor (IGF) system contributes to the initiation and progression of colon cancer remains poorly defined. We recently reported that a majority of human colon cancers express and secrete the potent mitogen IGF-II and at least two inhibitory binding proteins, IGFBP-2 and IGFBP-4. In the present study we measured the expression and secretion of IGF-II, IGFBP-2, and IGFBP-4 in relation to growth and differentiation of CaCo2 human colon cancer cells, which undergo spontaneous enterocytic differentiation in culture. Under the conditions of the present study, CaCo2 cells demonstrated an initial rapid phase of growth between Day 2 through days 7-9 of culture, followed by a significant retardation in the growth between days 9-13. Alkaline phosphatase (ALP) activity, a marker of enterocytic differentiation, progressively increased between Days 7-13 in culture, temporally correlating with post-confluent phase of negligible growth. These changes in growth and differentiation were accompanied by > 80% decline in the relative concentration of IGF-II messenger RNA (mRNA) between Days 2-13. In contrast, the relative mRNA concentrations of inhibitory binding proteins (IGFBP-2 and IGFBP-4) increased rapidly to 200% of Day 2 values by Days 5-7 before returning to baseline levels by Day 13. The relative protein concentrations of the three factors measured in the conditioned media of the cells followed a pattern very similar to that measured for the mRNA levels. While the changes in the relative protein concentrations and mRNA levels of IGF-II and IGFBP-4 were statistically significant, the changes measured in the RNA and protein levels of IGFBP-2 were not, as a result of large inter experimental variations. Thus these results suggested that CaCo2 cell differentiation may require an attenuation of IGF-II effects. To confirm the latter possibility, additional studies were conducted with a specific neutralizing antibody against IGF-II. Incubation of CaCo2 cells with anti-IGF-II antibodies from Day 0 through Day 7 significantly retarded the growth of the cells and was accompanied by a significant increase in the concentration of Alkaline phosphatase activity per 10(6) cells. Recently, we reported a potent inhibitory role of IGFBP-4 in the growth of colon cancer cells. In the present studies, a possible important role of IGF-II is illustrated not only in the growth but also in the differentiation of colonic cells. Our studies thus suggest that differential expression of IGF-II and IGFBPs may be playing a critical role in both proliferation and differentiation of colonocytes.

L3 ANSWER 13 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95340819 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7542277
TITLE: Cell polarity of the insulin-like growth factor system in

human intestinal epithelial cells. Unique apical sorting of insulin-like growth factor binding protein-6 in differentiated human colon cancer cells.

AUTHOR: Remacle-Bonnet M; Garrouste F; el Atiq F; Marvaldi J; Pommier G

CORPORATE SOURCE: Centre National de la Recherche Scientifique, Unite de Recherches Associee Proteines et Cancer, (URA CNRS-1924), Faculte de Medecine, Marseille, France.

SOURCE: The Journal of clinical investigation, (1995 Jul) Vol. 96, No. 1, pp. 192-200.
Journal code: 7802877. ISSN: 0021-9738.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199508

ENTRY DATE: Entered STN: 5 Sep 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 24 Aug 1995

AB In this study, we have used enterocyte-like differentiated HT29-D4 human colonic carcinoma cells cultured in a glucose-free medium (HT29-D4-GAL cells) on semi-permeable supports in order to investigate the polarity of the insulin-like growth factor (IGF) system. We report that these cells secrete endogenous IGF-II predominantly (66%) from the basolateral cell surface where type I IGF receptors are almost all (> 96%) localized. HT29-D4-GAL cells also secrete IGF-binding protein (IGFBP) - 2, -4, and -6 as evidenced by Western ligand and immunoblot analyses of conditioned medium. IGFBP-2 and IGFBP-4 are secreted primarily into the basolateral side (71 and 87%, respectively), whereas IGFBP-6 is targeted to the apical surface (76%) as a possible consequence of an active sorting. Finally, HT29-D4-GAL cells are found to display responses to IGF-II added to the basolateral but not the apical membrane side in terms of intracellular tyrosine phosphorylation and long-term stimulation of amino acid uptake. This study indicates (a) that IGF-II is potentially capable of autocrine regulation on the basolateral side of HT29-D4-GAL cell, and (b) that IGFBP-6 has a unique pattern of secretory polarity. It supports the concept that a differential sorting of the various forms of IGFBPs might play a modulatory role in the maintenance of a functional polarity in the differentiated HT29-D4-GAL cells.

L3 ANSWER 14 OF 14 MEDLINE on STN

ACCESSION NUMBER: 94237600 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7514152

TITLE: Alterations in serum levels of insulin-like growth factors and insulin-like growth-factor-binding proteins in patients with colorectal cancer.

AUTHOR: el Atiq F; Garrouste F; Remacle-Bonnet M; Sastre B; Pommier G

CORPORATE SOURCE: Laboratoire d'Immunologie, Faculte de Medecine, Marseille, France.

SOURCE: International journal of cancer. Journal international du cancer, (1994 May 15) Vol. 57, No. 4, pp. 491-7.
Journal code: 0042124. ISSN: 0020-7136.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199406

ENTRY DATE: Entered STN: 21 Jun 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 16 Jun 1994

AB It has been reported that insulin-like growth factor (IGF) II is

associated with human primary colorectal tumors and colon -carcinoma cell lines. Here, we examine alterations in circulating levels of IGFs and IGF binding proteins (IGFBPs) in patients with colorectal carcinoma, and compare them to age- and nutrition-adjusted references. We report (i) an increase in serum IGF-II concentrations (about 2-fold), whereas IGF-I concentrations are regarded as normal when aging is taken into account; (ii) an apparent increase in serum IGFBP-3 levels when compared to those of healthy elderly subjects, IGFBP-3 only being detected in the 150-kDa IGFBP ternary complex as in normal serum; (iii) abnormally elevated serum IGFBP-2 levels taking into account the apparent concentrations of IGFBP-3. This simultaneous elevation of IGFBP-3 and IGFBP-2 in the serum of patients with colorectal tumors appears to be unique in that it reflects a break in the inverse relationship between the serum IGFBP-3 and IGFBP-2 levels that is observed in normal and in several physiopathological conditions. Moreover, it enables a distinction to be made between 76.5% (13/17) of patients with colorectal carcinoma and normal adults, age-related healthy aged and malnourished patients. We propose that the disturbed serum IGFBP profile observed in the patients with colorectal cancer may be a consequence of oversecretion of IGF-II by the tumor cells. The usefulness of IGFs and IGFBPs as potential colorectal tumor-associated metabolic markers should be further investigated.

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OR IGFBP-2

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L3 116 L2 AND CANCER

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L4 ANSWER 40 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN
ACCESSION NUMBER: 1999:292985 BIOSIS
DOCUMENT NUMBER: PREV199900292985
TITLE: Altered levels of serum insulin-like growth factors in
patients with colorectal tumours.
AUTHOR(S): Renehan, A. [Reprint author]; Painter, J.; Potten, C. S.;
O'Dwyer, S. T.; Shalet, S. M. [Reprint author]
CORPORATE SOURCE: Department of Endocrinology, Christie Hospital NHS Trust,
Manchester, UK
SOURCE: Journal of Endocrinology, (March, 1999) Vol. 160, No.
SUPPL., pp. P113. print.
Meeting Info.: 18th Joint Meeting of the British Endocrine
Societies. Bournemouth, England, UK. April 12-15, 1999.
British Endocrine Societies.
CODEN: JOENAK. ISSN: 0022-0795.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 1999
Last Updated on STN: 5 Aug 1999

L4 ANSWER 41 OF 56 MEDLINE on STN
ACCESSION NUMBER: 1999382656 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10453284
TITLE: Epigenetic mechanisms for progression of prostate
cancer.
AUTHOR: Rennie P S; Nelson C C
CORPORATE SOURCE: Department of Surgery, University of British Columbia,
Vancouver, Canada.
SOURCE: Cancer metastasis reviews, (1998-1999) Vol. 17, No. 4, pp.
401-9. Ref: 76
Journal code: 8605731. ISSN: 0167-7659.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999
Entered Medline: 12 Oct 1999

AB Epigenetic mechanisms may be the main driving force for critical changes in gene expression that are responsible for progression of prostate cancers. The three most extensively characterized mechanisms for epigenetic gene-regulation are (i) changing patterns of DNA methylation, (ii) histone acetylations/deacetylations, and (iii) alterations in regulatory feedback loops for growth factors. Several studies have indicated that DNA hypermethylation is an important mechanism in prostate cancer for inactivation of key regulatory genes such as E-cadherin, pi-class glutathione S-transferase, the tumor suppressors CDKN2 and PTEN, and IGF-II. Similarly, histone acetylations and deacetylations are frequently associated respectively with transcriptional activation (e.g. IGFBP-2 and p21) and repression (e.g. Mad:Max dimers) of genes linked to prostate cancer progression. Recently, histone acetyltransferase and deacetylase activities have been shown to be intrinsic with transcriptional coregulator proteins that bind to steroid receptors (e.g. SRC-1 and PCAF). Changes in regulatory feedback loops for growth factors with prostate cancer progression tend toward shifts from paracrine to autocrine control where the receptor and ligand are produced by the same cell. While there are several examples of this progression pattern in prostate tumors such as with IGF, FGF, TGF-alpha and their respective receptors, the precise mechanism (i.e. epigenetic or mutational) is less certain. In the context of treatment options, the contribution of mutational versus epigenetic events to prostate cancer progression is an important consideration. Irreversible genetic changes are likely to be less amenable to therapeutic control than are epigenetic ones.

L4 ANSWER 42 OF 56 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1998383955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9719450
TITLE: Influence of treatment with onapristone on the IGF-system in breast cancer patients.
AUTHOR: Helle S I; Jonat W; Giurescu M; Ekse D; Holly J M; Lonning P E
CORPORATE SOURCE: Department of Oncology, Haukeland University Hospital, Bergen, Norway.
SOURCE: The Journal of steroid biochemistry and molecular biology, (1998 Aug) Vol. 66, No. 3, pp. 159-63.
Journal code: 9015483. ISSN: 0960-0760.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998
Entered Medline: 3 Sep 1998

AB The influence of the novel antiprogestin onapristone on the serum insulin-like growth factor (IGF) system was studied in a group of 13 postmenopausal women with metastatic breast cancer. Blood samples were obtained before treatment and subsequently after 1, 2 and 3 months on therapy. IGF-I, IGF-II and IGF-binding protein (IGFBP)-2 were measured by radioimmunoassay (RIA). In addition, the IGFBP profile was evaluated by Western ligand blotting (WLB), and IGFBP-3 fragmentation determined by immunoblotting. A moderate (29%) but significant increase in IGF-I was observed after 3 months on treatment ($p < 0.05$). IGFBP-2 showed a significant, progressive

increase during treatment when evaluated both by WLB (44% increase over baseline at 3 months) and by RIA (33% increase over baseline at 3 months). There was a non-significant trend towards an initial decrease in IGFBP-3 fragmentation. No significant alterations were observed in IGF-II or any of the binding proteins (except IGFBP-2) determined by Western ligand blotting. Due to the observation that onapristone treatment caused a moderate suppression of serum cortisol and androstenedione, we postulate the observed increase in IGF-I to be due to a slight glucocorticoid agonistic effect of the drug. On the contrary, the increase in IGFBP-2 may be related to disease progression as has been observed in patients suffering from prostatic cancer.

L4 ANSWER 43 OF 56 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 97358192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9215312
TITLE: Elevated serum insulin-like growth factor-binding protein 2 (IGFBP-2) and decreased IGFBP-3 in epithelial ovarian cancer : correlation with cancer antigen 125 and tumor-associated trypsin inhibitor.
AUTHOR: Flyvbjerg A; Mogensen O; Mogensen B; Nielsen O S
CORPORATE SOURCE: Institute of Experimental Clinical Research, Aarhus Kommunehospital, Aarhus University Hospital, Denmark.
SOURCE: The Journal of clinical endocrinology and metabolism, (1997 Jul) Vol. 82, No. 7, pp. 2308-13.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 13 Aug 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 7 Aug 1997

AB Insulin-like growth factors (IGFs) and IGF-binding proteins (IGFBPs) recently have been shown to play a physiological role in the female genital system, including the ovarian follicular system. However, little is known about the role of the IGF system in malignant ovarian disease. To assess possible mutual correlations between alterations in circulating IGFBP profiles and tumor markers in patients with epithelial ovarian cancer, we performed an RIA for IGFBP-2 and IGFBP-3 and a Western ligand blotting (WLB) in serum samples from 20 patients with epithelial ovarian cancer, 10 patients with benign ovarian tumors, and 8 healthy age-matched controls. The epithelial ovarian cancer group had a mean IGFBP-2 level that was 253% (RIA) and 105% (WLB) above that of controls. IGFBP-2 even correlated positively with the highly sensitive serum tumor marker, cancer antigen 125 (CA 125) ($r = 0.71$, $P < 0.001$) but not with the less sensitive tumor-associated trypsin inhibitor. In contrast, serum IGFBP-3 (by RIA and WLB) was decreased in patients with ovarian cancer, and IGFBP-3 proteolytic activity was detectable in some of the patients. Neither IGFBP-3 nor IGFBP-3 proteolytic activity correlated with CA 125; but the former correlated inversely, and the latter positively, with tumor-associated trypsin inhibitor. In conclusion, IGFBP-2 levels are high in serum of epithelial ovarian cancer patients, and the increment in serum IGFBP-2 correlates positively with CA 125. Alterations in serum IGFBP-2 levels may therefore, serve as a potential additional marker for ovarian cancer.

STN
ACCESSION NUMBER: 1998:69962 BIOSIS
DOCUMENT NUMBER: PREV199800069962
TITLE: Tamoxifen alters serum insulin-like growth factors and binding proteins in postmenopausal breast cancer patients. A prospective paired cohort study.
AUTHOR(S): Ho, G. H.; Ji, C. Y.; Phang, B. H.; Ng, E. H.
CORPORATE SOURCE: Dep. Surg., Singapore Gen. Hosp., Outram Road, Singapore 189608, Singapore
SOURCE: Breast Cancer Research and Treatment, (Oct., 1997) Vol. 46, No. 1, pp. 112. print.
Meeting Info.: 20th Annual San Antonio Breast Cancer Symposium. San Antonio, Texas, USA. December 3-6, 1997.
CODEN: BCTR6. ISSN: 0167-6806.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 20 Mar 1998

L4 ANSWER 45 OF 56 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 96241783 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8964854
TITLE: Effects of treatment with megestrol acetate, aminoglutethimide, or formestane on insulin-like growth factor (IGF) I and II, IGF-binding proteins (IGFBPs), and IGFBP-3 protease status in patients with advanced breast cancer.
AUTHOR: Frost V J; Helle S I; Lonning P E; van der Stappen J W; Holly J M
CORPORATE SOURCE: Department of Chemical Endocrinology, St. Bartholomew's Hospital, London, United Kingdom.
SOURCE: The Journal of clinical endocrinology and metabolism, (1996 Jun) Vol. 81, No. 6, pp. 2216-21.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 11 Dec 1996

AB The effects of treatment with the aromatase inhibitors aminoglutethimide (AG) and formestane or the synthetic progestin megestrol acetate (MA) on plasma levels of insulin-like growth factor I (IGF-I), IGF-II, IGF-binding proteins (IGFBPs), and IGFBP-3 protease status were investigated in 39 patients suffering from advanced breast cancer. Treatment with AG and MA elevated plasma levels of IGF-I by mean values of 27% ($n = 15$; $P < 0.025$) and 81% ($n = 7$; $P < 0.025$), respectively, whereas treatment with formestane had no effect ($n = 13$). Treatment with AG increased plasma levels of IGFBP-2, as evaluated by Western blotting ($P < 0.01$). MA caused a significant reduction in IGFBP-3 protease activity (mean reduction, 69%; $P < 0.05$). These alterations in plasma IGF-I and IGFBP-3 protease activity were reversed 4 weeks after terminating MA therapy ($n = 8$; $P < 0.025$). Taken together, 13 of 15 patients had reduced IGFBP-3 protease activity during treatment with MA compared to the control situation ($P < 0.0025$). Total levels of IGFBP-3 as measured by RIA were moderately elevated by treatment with MA (mean increase, 19%; $P < 0.05$), and Western immunoblotting revealed an increase in the amount of intact IGFBP-3 and reduced amounts of IGFBP-3 in the modified form. None of the treatment modalities had any influence on plasma levels of IGF-II. The increase in the plasma IGF-I concentration

seen during treatment with MA may be secondary to an increased level of intact IGFBP-3. This could reflect an alteration in IGF availability that contributes to the antitumor effect of MA.

L4 ANSWER 46 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:226298 CAPLUS
DOCUMENT NUMBER: 126:326645
TITLE: Secretion and expression of insulin-like growth factor binding protein-4 in benzo[a]pyrene resistant T47D5 human breast cancer cells
AUTHOR(S): Schrophe, Kathy; Moore, Michael; Safe, Stephen
CORPORATE SOURCE: Department Biochemistry Biophysics, Texas A and M University, College Station, TX, 77843, USA
SOURCE: Organohalogen Compounds (1996), 29, 367-370
CODEN: ORCOEP
PUBLISHER: ECO-INFORMA Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Secretion and function of insulin-like growth factor binding proteins (IGFBP) was investigated in estrogen receptor (ER)-pos. and aryl hydrocarbon (AH) receptor-neg. T47D human breast cancer cells (T47D5). Benzopyrene (I) resistant T47D clones (T47D5) were isolated by long term culturing wild-type T47D human breast cancer cells in I. Wild-type T47D cells secreted IGFBPs 2, 4, and 5. Secretion of IGFBP-4 was induced 1.5-fold by 17 β -estradiol (E2). TCDD decreased E2-induced secretion of IGFBP-4. T47D5 variant cells secreted lower levels of IGFBPs than wild-type cells. IGFBP-4 was secreted at 13-fold lower levels than in the T47D cells. Insulin-like growth factor induced proliferation of T47D5 cells only in the presence of media conditioned by T47D cells.

L4 ANSWER 47 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 95077543 EMBASE
DOCUMENT NUMBER: 1995077543
TITLE: Expression of growth factors and growth factor receptors in normal and tumorous human thyroid tissues.
AUTHOR: Van der Laan B.F.A.M.; Freeman J.L.; Asa S.L.
CORPORATE SOURCE: Department of Pathology, Mount Sinai Hospital, 600 University Avenue, Toronto, Ont. M5G 1X5, Canada
SOURCE: Thyroid, (1995) Vol. 5, No. 1, pp. 67-73. .
ISSN: 1050-7256 CODEN: THYRER
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 1995
Last Updated on STN: 29 Mar 1995
AB A number of growth factors have been implicated as stimuli of thyroid cell proliferation; overexpression of these growth factors and/or their receptors may play a role in the growth of thyroid tumors. To determine if immunohistochemical detection of growth factors and/or their receptors correlates with morphological alterations in proliferative lesions of thyroid, we examined the localization of epidermal growth factor (EGF), transforming growth factor- α (TGF- α) and their common receptor, EGF-receptor (EGF-R), insulin-like growth factor-1 (IGF-1), IGF-1-receptor (IGF-R) and IGF binding proteins (IGFBP)-1, -2, -3, and -4, nerve growth factor (NGF), and its receptor NGF-receptor (NGF-R), transforming growth factor- β (TGF- β), and basic fibroblast growth factor (bFGF), in normal thyroid tissue and various thyroid tumors. We applied the streptavidin-biotin technique to formalin-fixed, paraffin-embedded tissues. We studied 8-16 different cases of each of the following: normal human thyroid, multi-nodular

hyperplasia, follicular adenoma, papillary carcinoma, follicular carcinoma, medullary carcinoma, and anaplastic carcinoma. EGF, TGF- α , and their receptor EGF-R were widely expressed in normal thyroid and in all the thyroid lesions examined. IGF-1 and IGFBP-1 were diffusely present in all different thyroid tissues as well. There was no difference in staining intensity or distribution that correlated with the pathological process. IGFBP-4 seemed to have a variable expression. IGFBP-2 and -3 were detected only in medullary carcinomas. NGF immunoreactivity was found in thyroid tissues and tumors of all types; interestingly, NGF-R staining was found in the vascular stroma and immunoreactivity correlated with the degree of vascularization, but no staining was seen in normal or lesional thyroid cells. TGF- β expression was highly variable, whereas bFGF was not detected by this method in thyroid tissues. This study indicates that growth factors and growth factor receptors are expressed by thyroid follicular cells and C-cells. While they most likely play a role in cell regulation and proliferation in these tissues, their immunohistochemical profile does not correlate with the pathological condition.

L4 ANSWER 48 OF 56 MEDLINE on STN DUPLICATE '21
ACCESSION NUMBER: 95051313 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7525636
TITLE: Insulin-like growth factor axis abnormalities in prostatic stromal cells from patients with benign prostatic hyperplasia.
AUTHOR: Cohen P; Peehl D M; Baker B; Liu F; Hintz R L; Rosenfeld R G
CORPORATE SOURCE: Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania.
SOURCE: The Journal of clinical endocrinology and metabolism, (1994 Nov) Vol. 79, No. 5, pp. 1410-5.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 29 Jan 1996
Entered Medline: 21 Dec 1994
AB Benign prostatic hyperplasia (BPH) is a common proliferative disorder of unknown etiology. To assess whether patients with BPH have alterations in their prostatic IGF axis, we measured the expression (by Northern blotting) and the production (by Western ligand blotting and RIA) of insulin-like growth factor-II (IGF-II) and IGF-binding proteins (IGFBPs) in prostatic epithelial and stromal cell strains grown from normal ($n = 7$), hyperplastic ($n = 7$), and malignant ($n = 5$) surgical specimens. Levels of IGF-II messenger ribonucleic acid (mRNA; normalized for actin expression) were 10-fold higher in BPH stromal cell strains compared to those in normal stromal cell strains ($P < 0.0001$). Western ligand blotting of conditioned medium (CM) from normal stromal cells demonstrated the presence of IGFBP-2, -3, and -4. In the CM of BPH stromal cells, IGFBP-2 levels were dramatically reduced to less than 20% of normal ($P < 0.001$). Additionally, IGFBP-5, which was not observed in significant amounts in normal stromal cell-CM, was found in large quantities in BPH stromal cell-CM. Northern blot analysis of mRNA from normal and BPH stromal cells demonstrated a 5-fold decrease in IGFBP-2 mRNA ($P < 0.001$) and a 4-fold increase in IGFBP-5 mRNA ($P < 0.01$) in BPH compared to normal cells. In prostate stromal cells from cancer specimens, no abnormalities were found. No abnormalities were observed in the IGF axis parameters evaluated in prostate epithelial cells from BPH or cancer strains. We conclude that prostatic stromal cell strains isolated from patients with BPH hyperexpress the mRNA for IGF-II and

IGFBP-5 while expressing reduced amounts of IGFBP-2 mRNA. IGFBP, but not IGF-II, peptide levels in CM correspond to the mRNA differences. This is the first documentation of altered gene and protein expression in this common disease. We speculate that these abnormalities in the IGF axis may be important in the pathogenesis of BPH.

L4 ANSWER 49 OF 56 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 94237600 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7514152
TITLE: Alterations in serum levels of insulin-like growth factors and insulin-like growth-factor-binding proteins in patients with colorectal cancer.
AUTHOR: el Atiq F; Garrouste F; Remacle-Bonnet M; Sastre B; Pommier G
CORPORATE SOURCE: Laboratoire d'Immunologie, Faculte de Medecine, Marseille, France.
SOURCE: International journal of cancer. Journal international du cancer, (1994 May 15) Vol. 57, No. 4, pp. 491-7.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 21 Jun 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 16 Jun 1994

AB It has been reported that insulin-like growth factor (IGF) II is associated with human primary colorectal tumors and colon-carcinoma cell lines. Here, we examine alterations in circulating levels of IGFs and IGF binding proteins (IGFBPs) in patients with colorectal carcinoma, and compare them to age- and nutrition-adjusted references. We report (i) an increase in serum IGF-II concentrations (about 2-fold), whereas IGF-I concentrations are regarded as normal when aging is taken into account; (ii) an apparent increase in serum IGFBP-3 levels when compared to those of healthy elderly subjects, IGFBP-3 only being detected in the 150-kDa IGFBP ternary complex as in normal serum; (iii) abnormally elevated serum IGFBP-2 levels taking into account the apparent concentrations of IGFBP-3. This simultaneous elevation of IGFBP-3 and IGFBP-2 in the serum of patients with colorectal tumors appears to be unique in that it reflects a break in the inverse relationship between the serum IGFBP-3 and IGFBP-2 levels that is observed in normal and in several physiopathological conditions. Moreover, it enables a distinction to be made between 76.5% (13/17) of patients with colorectal carcinoma and normal adults, age-related healthy aged and malnourished patients. We propose that the disturbed serum IGFBP profile observed in the patients with colorectal cancer may be a consequence of oversecretion of IGF-II by the tumor cells. The usefulness of IGFs and IGFBPs as potential colorectal tumor-associated metabolic markers should be further investigated.

L4 ANSWER 50 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:529271 CAPLUS
DOCUMENT NUMBER: 121:129271
TITLE: Coculture inserts possess an intrinsic ability to alter growth regulation of human breast cancer cells
AUTHOR(S): Perachiotti, A.; Darbre, P. D.
CORPORATE SOURCE: Department of Biochemistry and Physiology, University of Reading, Reading, RG6 2AJ, UK
SOURCE: Experimental Cell Research (1994), 213(2), 404-11
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Coculture systems are used for a wide variety of cell-cell communication studies. The results reported here reveal that the microporous polycarbonate membranes used in the coculture inserts can remove inhibitory biol. macromols., resulting in increased cell growth. This provides a cautionary tale to all who use such coculture systems. For estrogen-sensitive breast cancer cells, the use of such membranes results in an increased growth in the absence but not in the presence of estradiol. These effects occurred reproducibly both in the presence of serum and in serum-free medium. Using MCF7 McGrath human breast cancer cells, the up-regulation of basal cell growth in the presence of the coculture insert and serum could be reduced upon blockade of the type I insulin-like growth factor receptor. Ligand blotting expts. revealed that these insert membranes could bind out insulin-like growth factor binding proteins (IGFBP) and remove IGFBP from the culture medium. This suggests a role for IGFBP in the regulation of MCF7 breast cancer cell growth. The mol. and clin. implications are discussed.

L4 ANSWER 51 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:677658 CAPLUS
DOCUMENT NUMBER: 121:277658
TITLE: The IGF axis in prostatic disease
AUTHOR(S): Cohen, Pinchas; Peehl, Donna M.; Bhala, Ajay; Dong, Gangi; Hintz, Raymond L.; Rosenfeld, Ron G.
CORPORATE SOURCE: School Medicine, University Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: International Congress Series (1994), 1056(INSULIN-LIKE GROWTH FACTORS AND THEIR REGULATORY PROTEINS), 369-77
CODEN: EXMDA4; ISSN: 0531-5131

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 18 refs. The insulin-like growth factor (IGF) axis is a multi-component network of mols. involved in the regulation of cell growth. The axis includes two major ligands, (IGF-I and IGF-II), cell surface receptors, (the type 1 IGF receptor family as well as the type 2 IGF receptor), a family of high affinity binding proteins which regulate IGF availability to the receptors, (the IGFBPs), and a group of IGFBP proteases which cleave IGFBPs and modulate IGF action. We have studied the role of the IGF axis in the autocrine-paracrine control of normal and neoplastic prostatic cell growth. Human seminal plasma contains IGFs, IGFBPs and IGFBP protease activity. A prostatic source for these IGF-axis mols. is likely. We have demonstrated the human prostate to contain all the elements of a functional IGF system. Prostate stromal cells in primary culture (PC-S) express mRNA for IGF-II and produce high mol. weight (15 kDa) IGF-II peptide in biol. active concns. Prostate epithelial cells in primary culture (PC-E) and PC-S express the type 1 IGF receptor. PC-E also produce IGFBP-2 and -4, (on both mRNA and peptide levels), while PC-S secrete IGFBP-2, -3 and -4. PC-E are exquisitely sensitive to the mitogenic effects of IGFs. Addnl., prostate specific antigen (PSA), secreted from PC-E in vivo and found in seminal plasma, can function as a potent IGFBP protease. PSA proteolysis reduces the affinity of IGFBP-3 to IGFs and can remove the inhibitory effects of IGFBP-3 on IGF induced PC-E growth. We have been able to identify several abnormalities in the IGF axis in the serum of patients with prostate cancer. Compared to age matched controls, serum from patients with prostate cancer displayed elevations of IGFBP-2 levels, as well as reduction of intact IGFBP-3 levels associated with a serum IGFBP-3 protease activity which is distinct from PSA. However, PC-E and PC-S from cancer sources showed no differences in the expression of IGF axis mols. relative to normal prostate cells. Finally, when PC-S from patients with benign prostatic hypertrophy (BPH) were compared to normals, several IGF axis mols. were

abnormally expressed. Ten-fold hyper-expression of the mRNA for IGF-II was noted, but was not associated with increased IGF-II peptide secretion. PC-S BPH IGFBP-2 peptide and mRNA levels were significantly decreased. CM from BPH PC-S displayed the presence of a 29 kDa IGFBP-5 doublet not seen in normal PC-S CM. These cells also displayed increased levels of the mRNA for the type 1 IGF receptor. These observations suggest that alterations to the prostatic IGF axis in BPH patients may be involved in the pathogenesis of abnormal stromal-epithelial interactions contributing to the development of BPH.

L4 ANSWER 52 OF 56 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 93232129 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7682560
TITLE: Elevated levels of insulin-like growth factor-binding protein-2 in the serum of prostate cancer patients.
AUTHOR: Cohen P; Peehl D M; Stamey T A; Wilson K F; Clemons D R; Rosenfeld R G
CORPORATE SOURCE: Department of Pediatrics, Stanford University Medical Center, California 94305.
CONTRACT NUMBER: AG-02231 (NIA)
DK-28229 (NIDDK)
SOURCE: The Journal of clinical endocrinology and metabolism, (1993 Apr) Vol. 76, No. 4, pp. 1031-5.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 4 Jun 1993
Last Updated on STN: 29 Jan 1996
Entered Medline: 18 May 1993

AB We have previously documented the presence of specific insulin-like growth factor (IGF)-binding protein (IGFBPs) in seminal plasma and prostate epithelial cell-conditioned medium IGFBP-2 is the prevalent IGFBP in both fluids. To assess whether patients with prostate carcinoma have alterations in serum IGFP levels related to the production of IGFBPs by their tumors, we performed Western ligand blots (WLB) and IGFBP-2 RIA on serum samples from 32 patients with prostate carcinoma of various degrees of clinical severity and compared them to results in 16 healthy age-matched controls. We have also measured serum IGF-I and -II by RIA. The mean level of IGFBP-2 in the prostate cancer patients was 170% of control levels by WLB analysis and 195% of control levels by RIA ($P < 0.01$). The degree of elevation of IGFBP-2 was related to the stage of the tumor and the levels of the serum tumor marker, prostate-specific antigen. Serum IGFBP-3 levels determined by WLB and serum IGF-I and IGF-II levels measured by RIA after acid chromatography were not different among the subjects with cancer and the normal controls. We conclude that IGFBP-2, which is the main IGFBP produced by prostate epithelial cells, is elevated in the serum of patients with prostate carcinoma, and that the degree of this elevation is related to serum prostate-specific antigen levels and the stage of the tumor. We speculate that prostate-derived IGFBPs may be secreted by prostate tumors and could be of value in understanding the pathophysiology of prostatic tumor growth as well as provide potential diagnostic markers.

L4 ANSWER 53 OF 56 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 93315594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7686915
TITLE: Serum insulin-like growth factor-binding protein-

2 (IGFBP-2) is increased and
IGFBP-3 is decreased in patients with prostate
cancer: correlation with serum prostate-specific
antigen.

AUTHOR: Kanety H; Madjar Y; Dagan Y; Levi J; Papa M Z; Pariente C;
Goldwasser B; Karasik A

CORPORATE SOURCE: Institute of Endocrinology, Chaim Sheba Medical Center,
Tel-Hashomer, Israel.

SOURCE: The Journal of clinical endocrinology and metabolism, (1993
Jul) Vol. 77, No. 1, pp. 229-33.
Journal code: 0375362. ISSN: 0021-972X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199308

ENTRY DATE: Entered STN: 20 Aug 1993
Last Updated on STN: 29 Jan 1996
Entered Medline: 6 Aug 1993

AB Insulin-like growth factors (IGFs) are potent mitogens that stimulate the growth of prostate cells. In serum, IGFs circulate bound to IGF-binding proteins (IGFBPs), which modulate their proliferative action. We studied the electrophoretic pattern of IGFBPs in the serum of patients with prostate cancer and in individuals with increased serum levels of prostate-specific antigen (PSA) in the absence of prostate malignancy. Serum IGFBP-2 was dramatically increased in patients with metastatic prostate cancer compared with healthy controls ($23.83 +/- 6.93\%$ vs. $2.95 +/- 0.52\%$ of total serum IGFBPs; $P < 0.02$). A moderate rise in IGFBP-2 was also observed among patients with increased PSA without malignancy. In contrast, a decrease in serum IGFBP-3 was detected in most patients with metastatic prostate cancer ($68.2 +/- 9.1\%$ vs. $95.4 +/- 0.9\%$ of total serum IGFBPs; $P < 0.02$) and was more pronounced in advanced cases. A highly significant correlation between serum IGFBP-2 and PSA levels was found ($r = 0.62$; $P < 0.002$), with a significant negative correlation between serum PSA and IGFBP-3 ($r = -0.63$; $P < 0.002$). We suggest that IGFBPs may be involved in growth modulation of prostate malignancy and that alterations in their serum levels may serve as a marker for prostate cancer.

L4 ANSWER 54 OF 56 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 93315589 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7686914
TITLE: Relationship between carbohydrate metabolism and serum insulin-like growth factor system in postmenopausal women: comparison of endometrial cancer patients with healthy controls.

AUTHOR: Rutanen E M; Stenman S; Blum W; Karkkainen T; Lehtovirta P;
Stenman U H

CORPORATE SOURCE: Department I Of Obstetrics and Gynecology, Helsinki
University Central Hospital, Finland.

SOURCE: The Journal of clinical endocrinology and metabolism, (1993
Jul) Vol. 77, No. 1, pp. 199-204.
Journal code: 0375362. ISSN: 0021-972X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199308

ENTRY DATE: Entered STN: 20 Aug 1993
Last Updated on STN: 29 Jan 1996
Entered Medline: 6 Aug 1993

AB Insulin is a major regulator of circulating insulin-like growth factor (IGF)-binding protein-1 (IGFBP-1), suppressing the hepatic production of

IGFBP-1. Postmenopausal age, obesity, hypertension, and impaired glucose tolerance, which are known risk factors for endometrial cancer, are all associated with hyperinsulinemia and insulin resistance. In this study, we investigated the relationship among serum insulin, glucose, insulin-like growth factors (IGF-I and IGF-II), and IGFBP-, -2, and -3 in 32 nondiabetic postmenopausal women with endometrial cancer and in 18 healthy controls. The mean fasting levels of glucose and insulin were higher, whereas the mean basal IGF-I, IGF-II, and IGFBP-3 levels were lower in the endometrial cancer patients than in the healthy control subjects. The mean fasting IGFBP-1 and IGFBP-2 levels did not differ between the groups, and no correlation was found between fasting insulin and IGFBP-1 concentrations or between insulin and IGFBP-2 concentrations in either of the study groups. During an oral glucose tolerance test, the mean glucose levels at 1 and 3 h as well as the mean insulin level at 3 h were significantly higher in the endometrial cancer patients than in the controls, and the area under the glucose curve was larger in the first group. An oral glucose load resulted in a similar fall in serum IGFBP-1 levels in endometrial cancer patients and controls (51% and 55% at 3 h). When the cancer patients were divided into two subgroups according to the body mass index (kilograms per m²), the obese group had higher glucose and insulin indices than the nonobese group. No difference was found by the same measures in healthy controls. The fasting serum IGFBP-1 levels tended to be lower in the obese than in the normal weight subjects, but the difference did not reach statistical significance. In summary, these results provide preliminary evidence that the inverse relation between fasting insulin and IGFBP-1, well established in children and young adults, disappears in elderly women, although short term suppression by insulin still occurs. Further, our data indicate that in addition to carbohydrate metabolism, postmenopausal women with endometrial cancer have alterations in their circulating IGF system compared to controls.

L4 ANSWER 55 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:205874 CAPLUS

DOCUMENT NUMBER: 118:205874

TITLE: Prostate-specific antigen (PSA) is an insulin-like growth factor binding protein-3 protease found in seminal plasma

AUTHOR(S): Cohen, Pinchas; Graves, Howard C. B.; Peehl, Donna M.; Kamarei, Mehdi; Giudice, Linda C.; Rosenfeld, Ron G.

CORPORATE SOURCE: Med. Cent., Stanford Univ., Stanford, CA, 94305, USA

SOURCE: Journal of Clinical Endocrinology and Metabolism
(1992), 75(4), 1046-53

CODEN: JCMAZ; ISSN: 0021-972X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB IGF binding protein-3 (IGFBP-3), the major serum carrier protein for the IGFs, is absent from Western ligand blots of seminal plasma, but is detectable by RIA. IGFBP-3 protease activity has recently been described in pregnancy serum. The possibility was examined that seminal plasma contains an IGFBP-3 protease, by incubating seminal plasma with ¹²⁵I-labeled human IGFBP-3. Seminal plasma had potent IGFBP-3 protease activity with a cleavage pattern different from that of pregnancy serum. Prostate-specific antigen (PSA) is a serine protease found in semen. Autoradiographs measuring IGFBP-3 protease activity demonstrated that purified PSA cleaved IGFBP-3, yielding a cleavage pattern identical to that of seminal plasma. IGFBP-2 and -4 in seminal plasma were not degraded by PSA. Cleavage of IGFBP-3 by PSA resulted in a marked reduction in the binding affinity of the fragments to IGF-I, but not IGF-II. PSA may thus serve to modulate IGF function within the reproductive system or in prostate cancer by altering IGF-IGFBP-3 interactions.

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ACCESSION NUMBER: 90333299 EMBASE
DOCUMENT NUMBER: 1990333299
TITLE: Regulation of binding proteins for insulin-like growth factors (IGF) in humans. Increased expression of IGF binding protein 2 during IGF I treatment of healthy adults and in patients with extrapancreatic tumor hypoglycemia.
AUTHOR: Zapf J.; Schmid C.; Guler H.P.; Waldvogel M.; Hauri C.; Futo E.; Hossenlopp P.; Binoux M.; Froesch E.R.
CORPORATE SOURCE: Metabolic Unit, Department of Medicine, University Hospital, CH-8091 Zurich, Switzerland
SOURCE: Journal of Clinical Investigation, (1990) Vol. 86, No. 3, pp. 952-961.
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB Insulin-like growth factors (IGFs) in blood form two complexes with specific binding proteins (BPs): a large, growth hormone (GH)-dependent complex with restricted capillary permeability, and a smaller complex, inversely related to GH, with high turnover of its IGF pool and free capillary permeability. The distribution of BPs and of IGFs I and II between these complexes was studied in sera from healthy adults treated with IGF I or/and GH and from patients with extrapancreatic tumor hypoglycemia. Like GH, IGF I administration raises IGF I and two glycosylation variants of IGFBP-3 in the large complex, but unlike GH drastically reduces IGF II. During IGF I infusion, IGFBP-3 appears in the small complex whose IGFBP-2 and IGF I increase three- to five-fold and five-fold, respectively. GH treatment, associated with elevated insulin levels, suppresses IGFBP-2 and inhibits its increase owing to infused IGF I. The small complex of tumor sera contains increased amounts of IGFBP-2 and -3, and two- to three-fold elevated IGF II. Conclusions: low GH and/or insulin during IGF I infusion and in extrapancreatic tumor hypoglycemia enhance expression of IGFBP-2 and favor partition of IGFBP-3 into the small complex. Free capillary passage and high turnover of its increased IGF I or II pools may contribute to compensate for suppressed insulin secretion during IGF I infusion or to development of tumor hypoglycemia.

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L4 ANSWER 30 OF 56 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001411993 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461068
TITLE: Alterations in the insulin-like growth factor system during treatment with diethylstilboestrol in patients with metastatic breast cancer.
AUTHOR: Helle S I; Geisler J; Anker G B; Leirvaag B; Holly J M; Lonning P E
CORPORATE SOURCE: Department of Oncology, Haukeland University Hospital, Bergen, N-5021, Norway.
SOURCE: British journal of cancer, (2001 Jul 20) Vol. 85, No. 2, pp. 147-51.
PUB. COUNTRY: Journal code: 0370635. ISSN: 0007-0920.
DOCUMENT TYPE: Scotland: United Kingdom
(CLINICAL TRIAL)

(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:
FILE SEGMENT:
ENTRY MONTH:
ENTRY DATE:

English
Priority Journals
200108
Entered STN: 27 Aug 2001
Last Updated on STN: 27 Aug 2001
Entered Medline: 23 Aug 2001

AB Alterations in the insulin-like growth factor (IGF)-system were evaluated in 16 patients treated with diethylstilboestrol 5 mg 3 times daily. Fasting blood samples were obtained before treatment and after 2 weeks, 1 month and/or 2-3 months on therapy. Insulin-like growth factor (IGF)-I, IGF-II, free IGF-I, IGF-binding protein (IGFBP)-1, IGFBP-2 and IGFBP-3 were measured by radioimmuno-/immunoradiometric-assays. All samples were subjected to Western ligand blotting as well as immunoblotting for IGFBP-3. We observed a significant decrease (percentage of pretreatment levels with 95 confidence intervals of the mean) in IGF-I [2 weeks 63% (49-79); 1 month 56% (44-73); 2-3 months 66% (53-82)], IGF-II [2 weeks 67% (56-80); 1 month 60% (52-68); 2-3 months 64% (55-75)], free IGF-I [2 weeks 29% (19-42); 1 month 25% (18-36); 2-3 months 31% (21-46)], IGFBP-2 [2 weeks 53% (18-156); 1 month 69% (61-78); 2-3 months 66% (57-78)], IGFBP-3 [2 weeks 74% (63-85); 1 month 69% (62-76); 2-3 months 71% (63-80)], as well as IGFBP-3 protease activity [2 weeks 71% (54-95); 1 month 78% (64-94); 2-3 months 71% (54-93)]. Contrary, the plasma levels (percentage of pretreatment levels with 95 confidence intervals of the mean) of IGFBP-1 [2 weeks 250% (127-495); 1 month 173% (138-542); 2-3 months 273% (146-510)] and IGFBP-4 [2 weeks 146% (112-192); 1 month 140% (116-169); 2-3 months 150% (114-198)] increased significantly. While this study confirms previous observations during treatment with oral oestrogens in substitution doses, the reduction in plasma IGF-II, free IGF-I, IGFBP-2 and -3 are all novel findings. A profound decrease in free IGF-I suggests a reduced bioavailability of IGFs from plasma to the tissues. These observations may be of significance to understand the mechanisms of the antitumour effect of diethylstilboestrol in pharmacological doses.

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L4 ANSWER 31 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:192392 BIOSIS
DOCUMENT NUMBER: PREV200100192392
TITLE: Energy balance and cancer: The role of insulin and insulin-like growth factor-I.
AUTHOR(S): Kaaks, R. [Reprint author]; Lukanova, A.
CORPORATE SOURCE: International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372, Lyon Cedex, 08, France
kaaks@iarc.fr
SOURCE: Proceedings of the Nutrition Society, (February, 2001) Vol. 60, No. 1, pp. 91-106. print.
CODEN: PNUSA4. ISSN: 0029-6651.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 2001
Last Updated on STN: 18 Feb 2002

AB Recent theories propose that a Western lifestyle may increase cancer risk through alterations in the metabolism of insulin and insulin-like growth factors (IGF; McKeown-Eyssen, 1994; Giovannucci, 1995; Kaaks, 1996; Werner and LeRoith, 1996). Insulin regulates energy metabolism, and increases the bioactivity of IGF-I, by enhancing its synthesis, and by decreasing several of its binding proteins (IGFBP; IGFBP-1 and -2). Insulin and IGF-I both stimulate anabolic processes as a function of available energy and elementary substrates (e.g. amino acids). The anabolic signals by insulin or IGF-I can promote

tumour development by inhibiting apoptosis, and by stimulating cell proliferation. Furthermore, both insulin and IGF-I stimulate the synthesis of sex steroids, and inhibit the synthesis of sex hormone-binding globulin (SHBG), a binding globulin (SHBG), a binding protein that regulates the bioavailability of circulating sex steroids to tissues. The present paper reviews epidemiological findings relating the risk of cancers of the colo-rectum, pancreas, breast, endometrium and prostate to body size (obesity, height) and physical activity, and discusses the relationships between obesity and physical activity and plasma levels of insulin, IGF-I and IGFBP. Subsequent sections review epidemiological findings relating cancer risk to indices of chronic hyperinsulinaemia, and to plasma levels of IGF-I and IGFBP. Conclusions are that chronic hyperinsulinaemia may be a cause of cancers of the colon, pancreas and endometrium, and also possibly of the breast. On the other hand, elevated plasma IGF-I, as total concentrations or relative to levels of IGFBP-3, appears to be related to an increased risk of prostate cancer, breast cancer in young women, and possibly colo-rectal cancer. For cancers of the endometrium, breast and prostate, these findings are discussed in the context of relationships between insulin and IGF-I and levels of bioavailable sex steroids.

L4 ANSWER 32 OF 56 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001077229 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11118044
TITLE: Identification of differentially expressed genes in human gliomas by DNA microarray and tissue chip techniques.
AUTHOR: Sallinen S L; Sallinen P K; Haapasalo H K; Helin H J; Helen P T; Schraml P; Kallioniemi O P; Kononen J
CORPORATE SOURCE: Department of Pathology, Tampere University Hospital, Finland.
SOURCE: Cancer research, (2000 Dec 1) Vol. 60, No. 23, pp. 6617-22.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 11 Jan 2001

AB New genomic large-scale screening techniques have made the task of establishing an accurate molecular fingerprint of cancer cells feasible. Here, we have used a two-phase strategy for identification of molecular alterations in gliomas. First, cDNA microarrays (Clontech Laboratories, Inc., Research Genetics) were used to pinpoint differentially expressed genes between normal brain and diffuse astrocytomas (grades II-IV), and between a primary tumor and a later tumor reoccurrence in the same patient. More than 200 gene expression alterations were detected from glioblastomas, whereas relatively few changes were seen in grade II and grade III tumors. The most distinct progression-related expression change was the up-regulation of the insulin-like growth factor binding protein 2 (IGFBP2) gene. Second, a high-density tissue microarray of 418 brain tumors was constructed and used for clinical validation of gene expression changes. Strong expression of IGFBP2 was associated with progression and poor patient survival in diffuse astrocytomas ($P < 0.0001$). Third, comparisons of the data between (a) multiple spots retrieved from one predefined tumor region (IGFBP2 and vimentin immunohistochemistry, 20 tumors) or between (b) standard slides and arrayed tissues (p53 immunohistochemistry, 42 tumors) revealed very little variation. In conclusion, the combined use of DNA microarrays and tissue microarrays offers a powerful strategy for rapid identification and thorough characterization of differentially expressed

genes in gliomas.

L4 ANSWER 33 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001025710 EMBASE

TITLE: Modifications of growth velocity and the insulin-like growth factor system in children with acute lymphoblastic leukemia: A longitudinal study.

AUTHOR: Arguelles B.; Barrios V.; Pozo J.; Munoz M.T.; Argente J.

CORPORATE SOURCE: Dr. J. Argente, Division of Pediatric Endocrinology, Laboratory of Research, Hospital Nino Jesus, Avenida. Menendez Pelayo 65, 28009 Madrid, Spain.
argentefen@teleline.es

SOURCE: Journal of Clinical Endocrinology and Metabolism, (2000) Vol. 85, No. 11, pp. 4087-4092. .
Refs: 33
ISSN: 0021-972X CODEN: JCMAZ

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
016 Cancer
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 8 Feb 2001
Last Updated on STN: 8 Feb 2001

AB The basis of impaired growth in children with acute lymphoblastic leukemia (ALL) is multifactorial, including the disease itself, infections, undernutrition, and adverse effects of therapy. Because growth is regulated by the GH-insulin-like growth factor (IGF) system, which may be altered in catabolic states, we studied serum IGF-I, free IGF-I, IGF-II, the IGF-binding proteins (IGFBP-1 to -3), and total and free acid-labile subunit (ALS) levels in 26 prepubertal children with ALL at diagnosis (n = 26) and 6 (n = 21), 12 (n = 21), 18 (n = 21), 24 (n = 20), 30 (n = 16), and 36 months (n = 16) after beginning treatment to investigate the effects of disease and therapy on this system and its relationship with growth in these patients. Intensive chemotherapy compromised growth, with a catch-up period beginning when maintenance therapy began and increased growth after stopping therapy. Weight increased 6 months after chemotherapy withdrawal, whereas the body mass index was increased both at 6 months after diagnosis and 6 months after therapy suppression. Serum IGF-I, IGF-II, IGFBP-3, and total and free ALS levels were significantly decreased at diagnosis. Normalization of IGF-II and IGFBP-3 occurred 6 months after diagnosis, and normalization of IGF-I and total and free ALS occurred 1 yr after terminating therapy. IGFBP-1 and IGFBP-2 levels were significantly increased at diagnosis and decreased after stopping therapy. Free IGF-I was elevated throughout the study. IGF and IGFBP-3 levels showed a close relationship to growth velocity at the end of chemotherapy, with this correlation remaining until at least 1 yr after therapy withdrawal. In conclusion, intensive chemotherapy compromises linear growth in prepubertal ALL patients, and this phenomenon is associated with alterations in the IGF system. However, when therapy is reduced or stopped, catch-up growth occurs, but various parameters of the GH-IGF axis remain impaired. This suggests the need for a longer period of follow-up to assess the long-term risks of therapy and disease on this system.

L4 ANSWER 34 OF 56 MEDLINE on STN DUPLICATE 12

ACCESSION NUMBER: 2000168606 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10706089

TITLE: Overexpression of insulin-like growth factor-binding protein-2 results in increased tumorigenic potential in Y-1 adrenocortical tumor cells.

AUTHOR: Hoeflich A; Fettscher O; Lahm H; Blum W F; Kolb H J;
Engelhardt D; Wolf E; Weber M M
CORPORATE SOURCE: Lehrstuhl fur Molekulare Tierzucht und
Haustiergenetik/Genzentrum, Ludwig-Maximilians-Universitat,
Munich, Germany.. hoeflich@lmb.uni-muenchen.de
SOURCE: Cancer research, (2000 Feb 15) Vol. 60, No. 4, pp. 834-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 30 Mar 2000
Last Updated on STN: 30 Mar 2000
Entered Medline: 20 Mar 2000

AB Increased concentrations of insulin-like growth factor-binding protein-2 (IGFBP-2) have been observed in human malignancies including adrenocortical carcinomas. To elucidate the functional consequences of IGFBP-2 overexpression, we have stably transfected the cDNA of murine IGFBP-2 in mouse adrenocortical tumor cells (Y-1). Long-term overexpression of IGFBP-2 was associated with significant morphological alterations, enhanced cell proliferation, and increased cloning efficiency as compared with mock transfected control cells. The enhanced proliferation of IGFBP-2 secreting clones was independent of exogenous insulin-like growth factors (IGFs). These data suggest that elevated levels of IGFBP-2 may contribute to the highly malignant phenotype of adrenocortical cancer by a thus far unknown, presumably IGF-independent, mechanism.

L4 ANSWER 35 OF 56 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1999413629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10485619
TITLE: Serum insulin-like growth factor (IGF)-I and IGF-binding proteins in lung cancer patients.
AUTHOR: Lee D Y; Kim S J; Lee Y C
CORPORATE SOURCE: Department of Pediatrics, Chonbuk National University Medical School, Chonju, Korea.
SOURCE: Journal of Korean medical science, (1999 Aug) Vol. 14, No. 4, pp. 401-4.
Journal code: 8703518. ISSN: 1011-8934.
PUB. COUNTRY: KOREA (SOUTH)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 1 Nov 1999
Last Updated on STN: 1 Nov 1999
Entered Medline: 20 Oct 1999

AB Many studies have shown that insulin-like growth factors (IGF-I & IGF-II) are implicated in the autocrine and paracrine growth of various tumors. Alterations in serum IGFs and IGF-binding proteins (IGFBPs) profiles have been reported in lung cancer. In this study, we measured serum levels of IGF-I and IGFBPs in 41 patients with lung cancer (small cell lung cancer, SCLC, 9; non-small cell lung cancer, NSCLC, 32) by radioimmunoassay and Western ligand blot (WLB). The serum IGF-I level in patients with lung cancer was significantly lower than in controls (207.9+/-62.6 vs 281.3+/-53.9 ng/mL, p<0.01). Patients with NSCLC showed significantly lower serum levels of IGF-I compared with SCLC patients (194.0+/-62.9 vs 258.4+/-27.8 ng/mL, p<0.01). Patients with squamous cell carcinoma tended to show lower serum levels of IGF-I than in those with adenocarcinoma (187.9+/-63.6 vs 215.9+/-59.5 ng/mL, p>0.05). The concentration of

IGFBP-3 in lung cancer was 48% of that found in controls by WLB. The serum level of IGFBP-2 was markedly elevated in patients with lung cancer compared with controls (1303.7+/-618.0 vs 696.2+/-300.5, p<0.01). However, there was no significant difference between SCLC and NSCLC groups. This result showed that serum level of IGF-I/IGFBPs may be useful markers for diagnosing and identifying tumor types in lung cancer and further studies are needed.

L4 ANSWER 36 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 14

ACCESSION NUMBER: 1999249356 EMBASE

TITLE: Epigenetic mechanisms for progression of prostate cancer.

AUTHOR: Rennie P.S.; Nelson C.C.

CORPORATE SOURCE: Dr. P.S. Rennie, Laboratory Research, Prostate Centre at VGH, Jack Bell Research Centre, 2660 Oak St., Vancouver, BC V6H 3Z6, Canada

SOURCE: Cancer and Metastasis Reviews, (1999) Vol. 17, No. 4, pp. 401-409. .
Refs: 76
ISSN: 0167-7659 CODEN: CMRED4

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19 Aug 1999
Last Updated on STN: 19 Aug 1999

AB Epigenetic mechanisms may be the main driving force for critical changes in gene expression that are responsible for progression of prostate cancers. The three most extensively characterized mechanisms for epigenetic gene- regulation are (i) changing patterns of DNA methylation, (ii) histone acetylations/deacetylations, and (iii) alterations in regulatory feedback loops for growth factors. Several studies have indicated that DNA hypermethylation is an important mechanism in prostate cancer for inactivation of key regulatory genes such as E-cadherin, pi-class glutathione S-transferase, the tumor suppressors CDKN2 and PTEN, and IGF-II. Similarly, histone acetylations and deacetylations are frequently associated respectively with transcriptional activation (e.g. IGFBP-2 and p21) and repression (e.g. Mad:Max dimers) of genes linked to prostate cancer progression. Recently, histone acetyltransferase and deacetylase activities have been shown to be intrinsic with transcriptional coregulator proteins that bind to steroid receptors (e.g. SRC-1 and PCAF). Changes in regulatory feedback loops for growth factors with prostate cancer progression tend toward shifts from paracrine to autocrine control where the receptor and ligand are produced by the same cell. While there are several examples of this progression pattern in prostate tumors such as with IGF, FGF, TGF- α and their respective receptors, the precise mechanism (i.e. epigenetic or mutational) is less certain. In the context of treatment options, the contribution of mutational versus epigenetic events to prostate cancer progression is an important consideration. Irreversible genetic changes are likely to be less amenable to therapeutic control than are epigenetic ones.

L4 ANSWER 37 OF 56 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 1999180639 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9924191

TITLE: Vitamin D analogue EB1089-induced prostate regression is associated with increased gene expression of insulin-like growth factor binding proteins.

AUTHOR: Nickerson T; Huynh H

CORPORATE SOURCE: Lady Davis Institute for Medical Research, McGill University, 3755 Cote Ste Catherine Road, Montreal, Quebec, Canada H3T 1E2.
SOURCE: The Journal of endocrinology, (1999 Feb) Vol. 160, No. 2, pp. 223-9.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 4 May 1999
Last Updated on STN: 4 May 1999
Entered Medline: 21 Apr 1999

AB Vitamin D analogues have an antiproliferative effect on prostate cancer cells in vitro and thus have been proposed as candidates for chemoprevention of prostate cancer. Insulin-like growth factor (IGF)-I has been shown to protect cells from apoptosis and plays an essential role in normal prostate physiology. We have studied the effects of the 1,25-dihydroxyvitamin D3 analogue EB1089 on the IGF system in the prostate in vivo. Treatment of rats with EB1089 for 14 days caused a 25% decrease in ventral prostate weight. Apoptosis was detected in prostate sections of EB1089-treated rats by terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay and histologic examination of hematoxylin/eosin stained tissue sections indicated that secretory epithelial cells were flattened, a characteristic of cells undergoing pressure-induced atrophy. Ventral prostate regression was associated with 15- to 25-fold increases in gene expression of IGF-binding proteins (IGFBPs)-2, -3, -4 and -5. We also observed a 40-fold increase in prostatic IGF-I mRNA levels in response to EB1089. Although we have previously shown that castration of rats leads to upregulation of IGFBPs in the ventral prostate, EB1089 treatment had no effect on serum levels of dihydrotestosterone or free testosterone. These results suggest that prostate regression induced by EB1089 may be related to alterations in availability of IGF-I as a result of increased production of IGFBPs.

L4 ANSWER 38 OF 56 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1999243391 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10226804
TITLE: Interleukin-1 alpha (IL-1 alpha) and tumor necrosis factor alpha (TNF alpha) regulate insulin-like growth factor binding protein-1 (IGFBP-1) levels and mRNA abundance in vivo and in vitro.
AUTHOR: Benbassat C A; Lazarus D D; Cichy S B; Evans T M; Moldawer L L; Lowry S F; Unterman T G
CORPORATE SOURCE: Department of Surgery, Cornell University Medical College, New York, USA.
CONTRACT NUMBER: DK41430-06 (NIDDK)
SOURCE: Hormone and metabolic research. Hormon- und Stoffwechselforschung. Hormones et metabolisme, (1999 Feb-Mar) Vol. 31, No. 2-3, pp. 209-15.
Journal code: 0177722. ISSN: 0018-5043.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 12 Jul 1999
Last Updated on STN: 12 Jul 1999
Entered Medline: 22 Jun 1999
AB TNF alpha and IL-1 alpha are thought to contribute to impaired anabolism in a variety of clinical states, including sepsis, cancer cachexia and the AIDS wasting syndrome. We asked whether cytokines exert

direct effects on hepatic production of IGFBP-1, an important modulator of IGF bioavailability. C57BL/6 mice were treated with 100 micrograms/kg of recombinant IL-1 alpha or TNF alpha by intraperitoneal injection. Western ligand blotting and immunoprecipitation with specific antisera revealed that serum levels of IGFBP-1 (but not IGFBP-2, -3, -4, -5 or -6) are increased approximately 4 fold 2 h after treatment and then decline. Northern blotting confirms that hepatic IGFBP-1 mRNA abundance also is increased acutely in both IL-1 alpha- and TNF alpha-treated animals. Similar results obtained in adrenalectomized mice indicate that adrenal activation is not required for this effect. Cell culture studies show that cytokines exert direct effects on the production of IGFBP-1 by HepG2 hepatoma cells, increasing IGFBP-1 levels in conditioned medium and the abundance of IGFBP-1 mRNA approximately 3-fold. In contrast, transient transfection studies with IGFBP-1 promoter/luciferase reporter gene constructs show that IGFBP-1 promoter activity is reduced after 18 hr cytokine treatment. We conclude that IL-1 alpha and TNF alpha increase circulating levels of IGFBP-1, reflecting direct effects on hepatic IGFBP-1 mRNA abundance. Stimulation of hepatic IGFBP-1 production may contribute to alterations in IGF bioactivity and impaired anabolism in clinical conditions where cytokine production is high. Additional studies are required to identify specific mechanisms mediating effects of cytokines on hepatic production of IGFBP-1.

L4 ANSWER 39 OF 56 MEDLINE on STN DUPLICATE 17
 ACCESSION NUMBER: 1999321091 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10395168
 TITLE: Changes in the secretion of insulin-like growth factor binding proteins -2 and -4 associated with the development of tamoxifen resistance and estrogen independence in human breast cancer cell lines.
 AUTHOR: Maxwell P; van den Berg H W
 CORPORATE SOURCE: Department of Oncology, The Queen's University of Belfast, Belfast City Hospital, UK.
 SOURCE: Cancer letters, (1999 May 24) Vol. 139, No. 2, pp. 121-7.
 Journal code: 7600053. ISSN: 0304-3835.
 PUB. COUNTRY: Ireland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199907
 ENTRY DATE: Entered STN: 6 Aug 1999
 Last Updated on STN: 6 Aug 1999
 Entered Medline: 23 Jul 1999
 AB We investigated the secretion of insulin-like growth factor binding proteins (IGFBPs) by estrogen-dependent ZR-75-1 and MCF-7 human breast cancer cells, and tamoxifen-resistant (ZR-75-9al and LY2) and estrogen-independent (ZR-PR-LT) variants which express altered levels of IGF-I receptor. IGFBP species (35 kDa and 44 kDa) were detectable in conditioned serum-free medium (SFM) by immunoblotting and positively identified as IGFBP-2 and -3, respectively. Secretion of IGFBP-2 into SFM by the tamoxifen-resistant and estrogen-independent cell lines was markedly reduced and secretion into SFM of the 24-kDa species, assigned the identity of IGFBP-4, was also reduced in the tamoxifen-resistant lines. There was no clear correlation between patterns of IGFBP secretion and IGF-I receptor expression.

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L4 ANSWER 20 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
 STN DUPLICATE 6

ACCESSION NUMBER: 2003:563264 BIOSIS
 DOCUMENT NUMBER: PREV200300564415
 TITLE: Effects of dietary intervention on IGF-I and IGF-binding proteins, and related alterations in sex steroid metabolism: The Diet and Androgens (DIANA) Randomised Trial.
 AUTHOR(S): Kaaks, R. [Reprint Author]; Bellati, C.; Venturelli, E.; Rinaldi, S.; Secreto, G.; Biessy, C.; Pala, V.; Sieri, S.; Berrino, F.
 CORPORATE SOURCE: Hormones and Cancer Group, International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372, Lyon Cedex 08, France kaaks@iarc.fr
 SOURCE: European Journal of Clinical Nutrition, (September 2003) Vol. 57, No. 9, pp. 1079-1088. print.
 CODEN: EJCNEQ. ISSN: 0954-3007.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 3 Dec 2003
 Last Updated on STN: 3 Dec 2003

AB Objective: To assess the effects of a comprehensive change in dietary composition on endogenous hormone metabolism. The specific aim was to examine whether this intervention could lead to favourable changes in insulin sensitivity, levels of IGF-I and IGF-binding proteins (IGFBPs), and total and bioavailable testosterone and estradiol, that would be expected to reduce breast cancer risk. Design: Randomised dietary intervention study; duration of 5 months. Subjects: From a total of 99 postmenopausal women, who had elevated baseline plasma testosterone levels, 49 women were randomly assigned to the dietary intervention arm and the other 50 to a control group. Interventions: Main aspects of the dietary intervention were reductions in the intake of total fat and refined carbohydrates, an increase in the ratio of n-3 over n-6 plus saturated fatty acids, and increased intakes of foods rich in dietary fibre and phytoestrogens. Results: Relative to the control group, women of the intervention group showed a significant reduction of body weight, waist circumference, fasting serum levels of testosterone, C peptide, glucose, and insulin area after glucose tolerance test, and a significant increase of serum levels of sex hormone-binding globulin, IGFBP-1, -2, and growth hormone-binding protein. Serum levels of IGF-I did not change. Conclusion: This comprehensive dietary intervention strategy proved to be successful in inducing changes in endogenous hormone metabolism that might eventually result in reduced breast cancer risk. Additional studies are needed to show whether the dietary intervention and related hormonal changes can be both maintained over longer periods, of at least

several years.

L4 ANSWER 21 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004022327 EMBASE
TITLE: Increased Activity of Catalase in Tumor Cells Overexpressing IGFBP-2.
AUTHOR: Hoeflich A.; Fetscher O.; Preta C.; Lahm H.; Kolb H.J.; Wolf E.; Weber M.M.
CORPORATE SOURCE: A. Hoeflich, Lehrst. Molec. Tierzucht Biotech., Ludwig-Maximilians-Universitat, Feodor-Lynen-Strasse 25, 81377 Munchen, Germany. hoeflich@lmb.uni-muenchen.de
SOURCE: Hormone and Metabolic Research, (2003) Vol. 35, No. 11-12, pp. 816-821. .
Refs: 29
ISSN: 0018-5043 CODEN: HMMRA2
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004
AB Elevated levels of IGFBP-2 are found in serum and tissues under various stressful conditions and in many malignancies. In previous studies, we have shown that overexpression of IGFBP-2 results in increased tumorigenic potential in Y-1 mouse adrenocortical tumor cells, and that these effects are presumably mediated through IGF-independent mechanisms. Here, we show that highly proliferative IGFBP-2-overexpressing Y-1 cells, but not control Y-1 cells, grow to very high cell densities. In order to evaluate whether the increased cell densities in IGFBP-2-transfected Y-1 cells were accompanied by alterations in the oxidative stress system, we analyzed the effect of IGFBP-2 overexpression on the activity of various antioxidative enzymes in two malignant cell lines. Among the tested antioxidative enzymes (catalase, superoxide-dismutase, glutathione peroxidase, glutathione S-transferase), only catalase enzyme activity was significantly higher in IGFBP-2-transfected Y-1 mouse adrenocortical tumor cells and in IGFBP-2-transfected human colon tumor cells (Caco-2) compared to control-transfected Y-1 and Caco-2 cells and non-tumor 293 human epithelial cells. However, overexpression of catalase in malignant cells did not result in increased resistance to oxidative stress as measured by cell viability and protein oxidation after treatment of the cells with hydrogen peroxide. This might be due to an upregulation of the GST enzyme activity after treatment with H₂O₂ that we observed selectively in the control-transfected Y-1 cells and which might compensate for the higher catalase activity in the IGFBP-2 overexpressing cells. In summary, we found a strong and selective upregulation of the catalase activity in IGFBP-2 overexpressing malignant Y-1 and Caco-2 cell lines that might contribute to the highly malignant phenotype of IGFBP-2 overexpressing tumors through as yet unknown mechanisms.

L4 ANSWER 22 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:748010 CAPLUS
DOCUMENT NUMBER: 140:91578
TITLE: Role of insulin-like growth factor binding proteins (IGFBPs) in breast cancer proliferation and metastasis
AUTHOR(S): Giles, Erin D.; Singh, Gurmit
CORPORATE SOURCE: Hamilton Regional Cancer Centre, Hamilton, ON, Can.

SOURCE: Clinical & Experimental Metastasis (2003), 20(6),
481-487
CODEN: CEXMD2; ISSN: 0262-0898
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cancers of the breast, prostate, and lung commonly metastasize to the bone resulting in osteolysis, pathol. fracture, pain and significant clin. morbidity. To date, the reason for such selectivity in the site of metastasis remains largely unknown. The bone is a rich source of many chemokines and growth factors, including: insulin-like growth factor (IGF) I and II, transforming growth factor- β (TGF- β), interleukins, and tumor necrosis factor- α (TNF- α) [1]. We propose that exposure of breast cancer cells to the bone microenvironment results in alterations in gene expression that favor the growth and proliferation of tumor cells in the bone. To investigate this hypothesis, MDA-MB-231 breast carcinoma cells were exposed to bone-derived conditioned media (BDCM) generated by culturing fetal rat calvaria for 24 h under serum free conditions. Using cDNA microarray technol., we have identified the insulin-like growth factor family of binding proteins (IGFBPs) as genes whose expression profiles are consistently and significantly altered with exposure to this simulated bone environment in vitro, when compared to untreated controls. Our data suggests that the upregulation of IGFBP-3 seen with exposure to the bone microenvironment is directly linked to an increase in TGF- β mediated cell proliferation. Furthermore, this process appears to be functioning through an IGF-independent mechanism.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:231775 BIOSIS
DOCUMENT NUMBER: PREV200300231775
TITLE: Genetic alterations occurring after treatment of prostate cancer cells with an antisense androgen receptor oligonucleotide or bicalutamide.
AUTHOR(S): Eder, Iris E. [Reprint Author]; Haag, Petra [Reprint Author]; Mousses, Spyro; Basik, Mark; Bartsch, Georg; Klocker, Helmut
CORPORATE SOURCE: Innsbruck, Austria
SOURCE: Journal of Urology, (April 2003) Vol. 169, No. 4 Supplement, pp. 57. print.
Meeting Info.: 98th Annual Meeting of the American Urological Association (AUA). Chicago, IL, USA. April 26-May 01, 2003. American Urological Association.
CODEN: JOURAA. ISSN: 0022-5347.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 May 2003
Last Updated on STN: 14 May 2003

L4 ANSWER 24 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:33568 BIOSIS
DOCUMENT NUMBER: PREV200400031715
TITLE: CYTOTOXICITY AND GENE EXPRESSION INDUCED BY HISTONE DEACETYLASE INHIBITOR, TRICHOSTATIN A, ON HUMAN HEPATOMA CELLS .
AUTHOR(S): Chiba, Tetsuhiro [Reprint Author]; Yokosuka, Osamu [Reprint Author]; Fukai, Kenichi [Reprint Author]; Kojima, Hiroshige [Reprint Author]; Imazeki, Fumio [Reprint Author]; Saisho, Hiromitsu [Reprint Author]

CORPORATE SOURCE: Chiba-city, Japan
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner,
(2003) Vol. 2003, pp. Abstract No. S947. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA.
May 17-22, 2003. American Association for the Study of
Liver Diseases; American Gastroenterological Association;
American Society for Gastrointestinal Endoscopy; Society
for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004
AB Histone acetylation is one of the key factors in control of gene expression in mammalian cells. Histone deacetylase (HDAC) inhibitors has been reported to induce cell growth arrest, apoptosis and differentiation in cancer cells, however, the effect of HDAC inhibitor on hepatoma cells has not been well-recognized. In this study, we examined cell viability and gene expression profile in 4 hepatoma cell lines treated with HDAC inhibitor, trichostatin A (TSA). The MTT assay demonstrated that TSA had cytotoxic effects on all the hepatoma cell lines studied, in not only concentration-dependent but also time-dependent manner. Cell viability after 24h treatment with 200 ng/ml of TSA on HuH7, Hep3B, HepG2, and PLC/PRF/5 cells was 74.3%, 90.8%, 76.0% and 72.0%, respectively. Because cell viability of HepG2 with intact p53 showed little difference compared with other cell lines with impaired p53 function, the cytotoxic effect of TSA seemed to be independent of p53 function. The cDNA microarray consisting of 557 distinct cDNA of cancer-related genes have revealed that 9 genes including collagen type I alpha 2 (COL1A2), insulin-like growth factor binding protein 2 (IGFBP2), integrin alpha 7 (ITGA7), defender against cell death 1 (DAD1), basigin (BSG), quiescin Q6 (QSCN6), nerve growth factor receptor (NGFR), p53-induced protein (PIG11), and superoxide dismutase 3 (SOD3) exhibited the substantial induction (ratio >2.0) after TSA treatment in multiple cell lines. Chromatin immunoprecipitation (ChIP) assay using anti-acetylated histone H3 or H4 antibody showed that altered mRNA expression of these genes were proportional to increased levels of acetylation on histones, concordant with the cDNA microarray analysis. In conclusion, these results indicate HDAC inhibitors possess potential as a new therapeutic agent for hepatoma. It is also demonstrated that alteration in levels of histone acetylation plays an important role in transcriptional regulation on hepatoma cells..

L4 ANSWER 25 OF 56 MEDLINE on STN
ACCESSION NUMBER: 2002636463 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12394769
TITLE: Serum levels of insulin-like growth factor-1 and insulin-like growth factor-1 binding proteins after radical prostatectomy.
AUTHOR: Bubley Glenn J; Balk Steve P; Regan Meredith M; Duggan Stephen; Morrissey Mary Ellen; Dewolf William C; Salgami Ellena; Mantzoros Christos
CORPORATE SOURCE: Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA.
SOURCE: The Journal of urology, (2002 Nov) Vol. 168, No. 5, pp. 2249-52.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 26 Oct 2002

Last Updated on STN: 11 Dec 2002
Entered Medline: 25 Nov 2002

AB PURPOSE: Elevated serum levels of insulin-like growth factor-1 (IGF-1) have been consistently shown to be a risk factor for prostate cancer. Alterations in serum IGF-1 binding proteins 1 to 3 have also been associated with prostate cancer risk. A potentially important complication in these studies is that prostate tissue, perhaps especially malignant prostate tissue, may secrete IGF-1 and its binding proteins into serum. In fact, it is possible that altered levels of these proteins observed in subjects at risk for prostate cancer are the result of prostate cancer rather than related to its cause. MATERIALS AND METHODS: The contribution of prostate cancer to serum levels of IGF-1 and IGF-1 binding proteins was determined by analyzing serum samples from 86 patients with prostate cancer 2 weeks before and 8 weeks after radical prostatectomy. Preoperative and postoperative values for IGF-1 and its 3 major binding proteins were analyzed using univariate and multivariate analysis models. RESULTS: On univariate analysis significant increases and not decreases in IGF-1, IGF binding protein-1 and 3 were observed after prostatectomy. On multivariate analysis a significant post-prostatectomy increase was observed for IGF-1 binding proteins 1 and 3 but the increase in IGF-1 was not significant. CONCLUSIONS: Increased levels of IGF-1 and IGF-1 binding proteins were unexpected after prostatectomy. This result makes it extremely unlikely that secretion from the prostate, even if it contains cancer, affects serum levels of these proteins. The implication of these findings is that endocrine production of IGF-1 is a factor in prostate cancer risk. Therefore, strategies to lower serum IGF-1 may be potentially useful.

L4 ANSWER 26 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:948706 CAPLUS

DOCUMENT NUMBER: 138:219239

TITLE: Fasting glucose is a risk factor for breast cancer: a prospective study

AUTHOR(S): Muti, Paola; Quattrin, Teresa; Grant, Brydon J. B.; Krogh, Vittorio; Micheli, Andrea; Schunemann, Holger J.; Ram, Malathi; Freudenheim, Jo L.; Sieri, Sabina; Trevisan, Maurizio; Berrino, Franco

CORPORATE SOURCE: Department of Social and Preventive Medicine, University of Buffalo, State University of New York, Buffalo, NY, USA

SOURCE: Cancer Epidemiology, Biomarkers & Prevention (2002), 11(11), 1361-1368

CODEN: CEBPE4; ISSN: 1055-9965

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB There is some evidence that glucose and other factors related to glucose metabolism, such as insulin and insulin-like growth-factors (IGFs) may contribute to breast cancer development. The present study analyzed the hypothesis that serum glucose, insulin levels, and IGF-I pattern are associated with breast cancer using a nested case-control study. Between 1987 and 1992, 10,786 women ages 35-69 were recruited in a prospective study in Italy. Women with history of cancer and on hormone therapy were excluded at baseline. At recruitment, blood samples were collected after a 12-h fast between 7:30 and 9:00 a.m. from all of the study participants. After 5.5 yr, 144 breast cancer cases were identified among the participants of the cohort. Four matched controls were chosen for each breast cancer case from members of the cohort who did not develop breast cancer during the follow-up period. In premenopausal women, glucose was associated with breast cancer risk: the age, body mass index, and reproductive variable adjusted relative risk (RR) for the highest quartile of serum glucose vs. the lowest was 2.8 [95% confidence

interval (CI), 1.2-6.5], and P for trend was 0.02. Insulin showed a weaker association with breast cancer, the adjusted RR of the highest quartile vs. the lowest was 1.7 (95% CI, 0.7-4.1), and P for trend was 0.14, whereas the adjusted RR of the highest quartile of IGF-I was 3.1 (95% CI, 1.1-8.6), and P for trend was 0.01. Increased levels of insulin-like growth factor binding protein-3 (IGFBP)-3 were related to breast cancer risk: the adjusted RR for the highest quartile was 2.1 (95% CI, 0.95-4.75), and P for trend was 0.02. In postmenopausal women, the assocns. of glucose, insulin, and IGF-1 pattern were associated with breast cancer risk in heavier subjects characterized by a body mass index higher than 26. These results indicate that chronic alteration of glucose metabolism is related to breast cancer development.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 56 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002464114 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12223436
TITLE: Insulin-like growth factor II and colorectal cancer risk in women.
AUTHOR: Hunt Kelly J; Toniolo Paolo; Akhmedkhanov Arslan; Lukanova Annekatrin; Dechaud Henri; Rinaldi Sabina; Zeleniuch-Jacquotte Anne; Shore Roy E; Riboli Elio; Kaaks Rudolf
CORPORATE SOURCE: International Agency for Research on Cancer, 69372 Lyon Cedex 08, France.
SOURCE: Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, (2002 Sep) Vol. 11, No. 9, pp. 901-5.
Journal code: 9200608. ISSN: 1055-9965.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 12 Sep 2002
Last Updated on STN: 26 Feb 2003
Entered Medline: 25 Feb 2003

AB Recently, a number of prospective studies showed evidence that the growth hormone/insulin-like growth factor I (IGF-I) axis may be important in the development of colorectal cancer. However, only a few studies have reported on the possible relationship of colorectal cancer risk with circulating levels of IGF-II, which are not growth hormone dependent and which do not vary with alterations in energy balance. In a case-control study of 102 cases and 200 matched controls nested within a cohort of 14,275 women in New York, we examined the relationship between colorectal cancer risk and prediagnostic serum levels of IGF-II. Conditional logistic regression analysis showed an odds ratio (OR) for colorectal cancer of 2.02 (95% confidence interval (CI): 0.83-4.93), comparing the upper to lower quintile of IGF-II. This association was slightly attenuated after excluding IGF-II measurements in serum samples taken within 1 year before case diagnosis (OR of 1.81; 95% CI: 0.71-4.64) and moderately attenuated after excluding IGF-II measurements in serum samples taken within 2 years before case diagnosis (OR of 1.47; 95% CI: 0.56-3.91). Adjustment for IGF-1, IGF binding protein (BP)-1, IGFBP-3, smoking, or body mass index did not substantially alter the association, whereas adjustment for IGFBP-2 moderately attenuated the relationship. Our results confirm those of three recent case-control studies, and collectively these results suggest a possible increase in colorectal cancer risk among subjects with comparatively elevated serum IGF-II. Mechanisms that might cause the increase in IGF-II levels are unknown but may include loss of

parental imprinting of the IGF-II gene.

L4 ANSWER 28 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 8

ACCESSION NUMBER: 2002190423 EMBASE

TITLE: Elevated insulin-like growth factor-1 and insulin-like growth factor binding protein-2 in malignant pleural effusion.

AUTHOR: Olchovsky D.; Shimon I.; Goldberg I.; Shulimzon T.; Lubetsky A.; Yellin A.; Pariente C.; Karasik A.; Kanety H.

CORPORATE SOURCE: D. Olchovsky, Department of Medicine A, Chaim Sheba Medical Center, Tel-Hashomer 52621, Israel. dolcho@zahav.net.il

SOURCE: Acta Oncologica, (2002) Vol. 41, No. 2, pp. 182-187. .

Refs: 27

ISSN: 0284-186X CODEN: ACTOEL

COUNTRY: Norway

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 13 Jun 2002
Last Updated on STN: 13 Jun 2002

AB Insulin-like growth factor-1 (IGF-1) and its binding proteins (IGFBPs) are produced by many tissues and are present in serum and other biological fluids. Alterations in sera of IGF-1 and 2 and IGFBPs were demonstrated in patients with malignancy, infection and other diseases causing pleural effusion. In this study the IGF-1 and IGFBP-2 content and the specific electrophoretic patterns of IGFBPs in samples of sera and pleural effusions of 25 patients with malignancy, infection and congestive heart failure were investigated. IGF-1 levels in exudative effusions of malignant solid tumors were significantly higher [(mean \pm SD), 20.9 \pm 7.5 nmol/L, n = 9] than in lymphoma (11.0 \pm 5.2 nmol/L, n = 5; p < 0.05), infection (11.4 \pm 6.5 nmol/L, n = 6; p < 0.05) and transudative effusion of congestive heart failure (4.3 \pm 3.3 nmol/L, n = 5; p < 0.02). IGFBP-2 was markedly increased in effusions of malignant solid tumors (2.14 $<$ 0.82 mg/L, n = 9) compared with exudates of lymphoma, infection and transudates (1.10 \pm 0.70, 1.22 \pm 0.32 and 0.93 \pm 0.52 nmol/L, respectively, p < 0.05). Moreover, in effusion of solid tumors, IGFBP-2 levels were higher than those in corresponding sera, which suggests local production of this binding protein. The demonstration of IGFBP-2 in solid tumor cells by immunohistochemistry further supports this possibility. This work demonstrates the existence of the IGF-1/IGFBP system in pleural fluids from different etiologies and implies possible use of IGF-1 and IGFBP-2 as a potential marker of malignant effusions.

L4 ANSWER 29 OF 56 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 2002116684 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11836446

TITLE: Expression of components of the IGF signalling system in childhood acute lymphoblastic leukaemia.

AUTHOR: Vorwerk P; Wex H; Hohmann B; Mohnike K; Schmidt U; Mittler U

CORPORATE SOURCE: Department of Paediatric Oncology, Otto-von-Guericke-University Magdeburg, Emanuel-Larisch-Weg 17-19, D-39112 Magdeburg, Germany.. Peter.Vorwerk@medizin.uni-magdeburg.de

SOURCE: Molecular pathology : MP, (2002 Feb) Vol. 55, No. 1, pp. 40-5.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(MULTICENTER STUDY)
(CLINICAL TRIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20 Feb 2002
Last Updated on STN: 12 Mar 2002
Entered Medline: 11 Mar 2002

AB BACKGROUND: Alterations in the insulin-like growth factor (IGF) system have been reported for different tumours. They are of particular interest in the search for new prognostic and therapeutic approaches in cancer. In childhood acute lymphoblastic leukaemia (ALL) the amount of "tumour mass" at diagnosis can exceed 1 kg. To understand the endocrine, paracrine, and autocrine potential of the malignant transformed progenitor cells, the ability of these cells to express components of the IGF system needs to be investigated. AIM: To characterise the expression pattern of genes of the IGF system in malignant lymphoblasts of children suffering from ALL. METHODS: Reverse transcription polymerase chain reaction of Ficoll separated mononuclear cells from 142 children with ALL, 127 cord blood samples, and 55 blood samples of age matched controls were studied. RESULTS: The expression of IGF-I, IGF-II, IGF binding protein 5 (IGFBP-5), and CTGF (IGFBP-rP2) was seen in a higher proportion of mononuclear cells of patients with ALL than in controls. Patients with ALL who were in continuous remission had a lower percentage of IGFBP-2 and IGFBP-3 expressing mononuclear cells at diagnosis than did those who developed a relapse. Only malignant lymphoblasts of B cell origin showed expression of CTGF (IGFBP-rP2). Malignant lymphoblasts of T cell origin more often expressed IGFBP-2 and IGFBP-5, whereas IGF-II and IGFBP-3 expression was seen more often in lymphoblasts of B cell origin. CONCLUSIONS: Malignant lymphoblasts of patients with ALL express components of the IGF system and therefore promote their own growth in an autocrine, paracrine, or endocrine manner. Whether these components will be useful as prognostic factors in the stratification of ALL treatment in children needs to be evaluated.